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CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

Effects of Feeding Different Fats on Serum-cholesterol Level — B. BRONTE-STEWART, M.R.C.P.; A. ANTONIS, PH.D.; L. EALES, M.R.C.P.; Prof. J. F. BROCK, F.R.C.P. 521

Treatment of Tetanus — Prof. H. C. A. LASSEN, M.D.; ERIK HENRIKSEN, M.D.; FRITS NEUKIRCH, M.D.; H. S. KRISTENSEN, M.D. 527

Adrenalectomy for Vascular Disease of Diabetes — J. M. MALINS, M.R.C.P. 530

Tricuspid Valvotomy — ARTHUR HOLLMAN, M.R.C.P. 535

Treatment of Hay-fever with Hydrocortisone Snuff — H. HERXHEIMER, M.D.; MONICA MCALLEN, M.R.C.P. 537

Radcliffe Respiration Pumps — W. RITCHIE RUSSELL, F.R.C.P.; EDGAR SCHUSTER, D.SC.; A. CRAMPTON SMITH, F.F.A. R.C.S.; J. M. K. SPALDING, M.R.C.P. 539

Delayed Prothrombin Estimation — HAMISH WATSON, M.R.C.P.E. 541

Control of Hypotension Following Removal of Aortic Clamps — J. R. KENYON, F.R.C.S.; K. E. COOPER, M.B. 543

Reserpine in Anxiety States — E. H. HARE, M.D.; C. P. SEAGER, M.B.; A. LEITCH, M.D. 545

Acute and Latent Porphyria — S. R. F. WHITTAKER, F.R.C.P.; T. P. WHITEHEAD, F.R.I.C. 547

Diarrhœa Due to Phenolphthalein — J. M. FRENCH, M.D.; R. GADDIE, PH.D.; NADYA SMITH 551

PRELIMINARY COMMUNICATION

Treatment of Hypophosphatasia with Cortisone — D. FRASER, M.D.; J. C. LAIDLAW, F.R.C.P.(C.) 553

MEDICAL SOCIETIES

Association of Clinical Pathologists 554

LEADING ARTICLES

FATS AND DISEASE 557

A MERGER? 558

TREATMENT OF CORONARY THROMBOSIS 559

ANNOTATIONS

A New Muscle Relaxant 561

Mental Defect and Hypsarrhythmia 561

Tuberculosis After Partial Gastrectomy 561

Children Need Families 562

Ekiri 562

SPECIAL ARTICLES

Heroin: from the International Point of View — Prof. P. O. WOLFF, M.D. 563

Nutritional Studies in a Mental Hospital — Z. A. LEITNER, M.D.; I. C. CHURCH, M.R.C.S. 565

Family Planning Association 567

NEW INVENTIONS

Hallux Forceps — W. E. TUCKER, F.R.C.S. 555

SYMPOSIA

The Neurohypophysis 568

OCCASIONAL SURVEY

Eosinophils and the Spleen 569

PUBLIC HEALTH

Attendance at Child-welfare Centres — H. D. CHALKE, M.R.C.P. 571

Neonatal Mortality 574

LETTERS TO THE EDITOR

Deficiency of Essential Fatty Acids (Prof. Ancel Keys, PH.D.) 576

Vomiting Sickness in Jamaica (Dr. Cicely Williams) 577

Revision of the Curriculum (Prof. G. M. Wyburn, F.R.F.P.S.; Dr. J. V. Walker) 577

Eczema Vaccinatum (Dr. N. R. Grist) 578

A New Way of Treating Flat Feet in Children (Mr. A. J. Helfet, F.R.C.S.) 578

Myasthenia Gravis (Dr. H. C. Churchill-Davidson, Dr. A. T. Richardson) 578

Paratyphoid-C Osteomyelitis (Dr. Margaret E. Barton, Dr. D. R. Christie, Dr. K. Valteris) 579

Antenatal Detection of Hereditary Disorders (Dr. J. H. Edwards) 579

Perforated Acute and Chronic Peptic Ulcer (Mr. H. D. Moore, F.R.C.S.) 579

Recurrent Dislocation of the Shoulder (Mr. J. G. Bonnin, F.R.C.S.) 579

Breast Changes in Fibrocystic Disease of the Pancreas (Dr. J. C. Valentine) 580

Fluids for Intravenous Infusion (Dr. John Barnard) 580

Hæmatemesis (Mr. W. J. M. Brandon, F.R.C.S.E.) 580

Prevention of Renal Lesions Due to Ischæmia (Dr. P. V. Véghelyi, Dr. L. Hársing, Dr. K. László) 581

REVIEWS

Notices of Books 555

PARLIAMENT

Question Time 574

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents 575

OBITUARY

Arthur Hugh McCulloch Eaton 582

Alexander Gibson 582

NOTES AND NEWS

Forwards in Manchester 583

Hospital Administrative Staff 583

Health in Industry 583

Improving a Fireguard 583

A Brochure for the Young Patient 584

University of London 584

National University of Ireland 584

University of Dublin 584

Diary of the Week 582

Appointments 581

Births, Marriages, and Deaths 581

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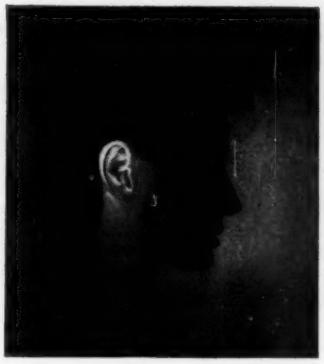

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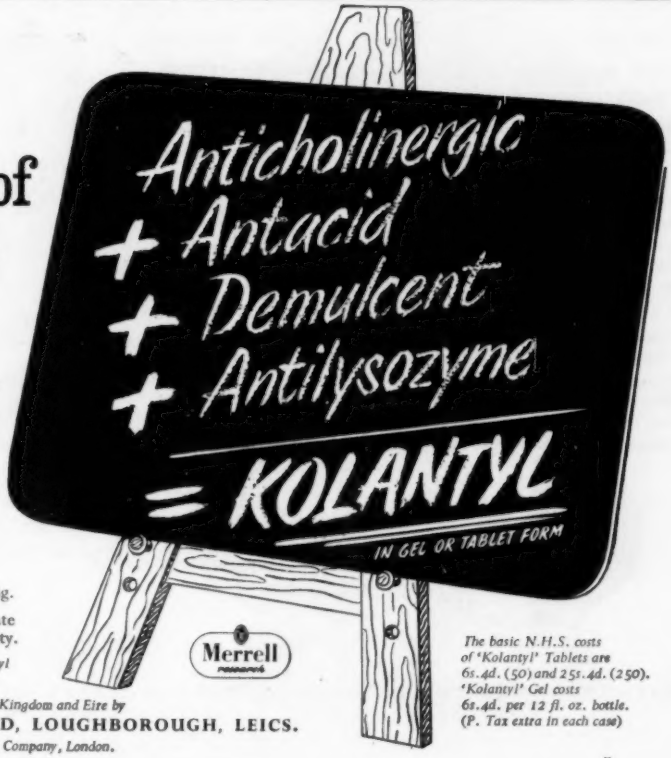

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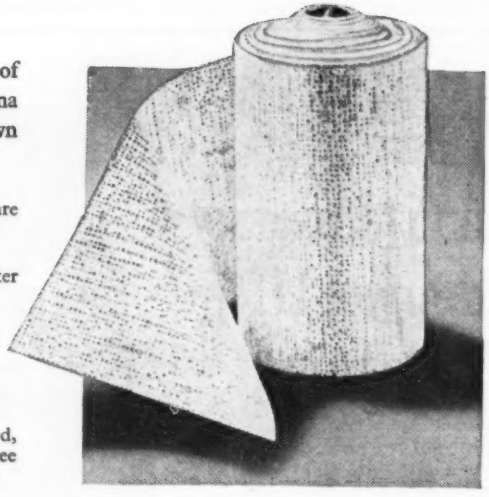

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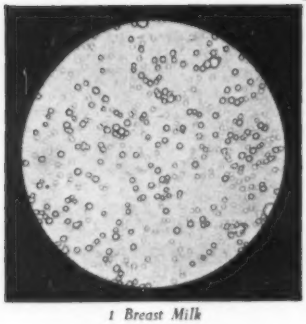

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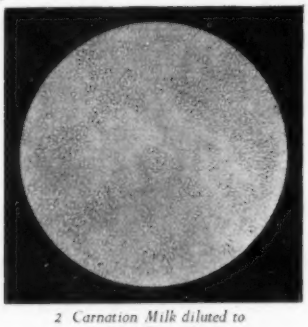

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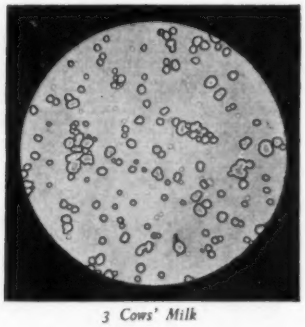

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The summary of the discussion appended to this report is as follows:

"Aspirin is a serious gastric irritant, particularly in peptic ulcer patients."

Here is a further extract from the report:— "In conclusion it is suggested that aspirin should never be given to patients with peptic ulceration, or indeed to those who have any gastric intolerance to it, however mild. Such an instruction should be given a prominent place in peptic ulcer advice charts, usually in place of much that could be safely left out. Some of these patients took aspirin on a full stomach only in powder form, with serious results, and, although this method almost certainly mitigates its irritant effects, it does not guarantee immunity. Calcium aspirin does not have this irritant action unless it has deteriorated through standing, and it can be used with impunity, especially if prescribed in soluble form. This simple measure would, in our opinion, cut down significantly, the incidence of haematemesis and exacerbations of ulcer symptoms."

SOLPRIN provides calcium aspirin in pure and stable form.

CODIS is a compound tablet that provides codeine and phenacetin and calcium aspirin, in place of the ordinary aspirin in Tab. Codein. Co. B.P.

Neither SOLPRIN nor CODIS is advertised to the public.

RECKITT AND COLMAN LTD., HULL & LONDON (PHARMACEUTICAL DEPT. HULL)

Preceptin
Simple, effective contraception
where secondary occlusive methods
are unacceptable or impracticable
Preceptin REG'D VAGINAL GEL
Ortho Pharmaceutical Limited · High Wycombe · England
Ortho

Boots

CORTISTAB and HYDROCORTISTAB preparations

These products are manufactured **in Great Britain** at our extensive plant, designed for the large scale production of corticosteroids.

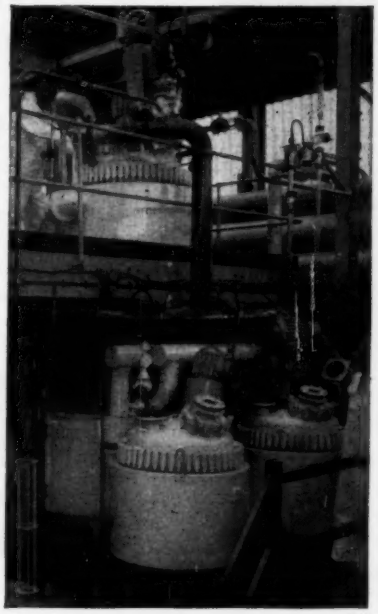
CORTISTAB (CORTISONE ACETATE)

TABLETS 25 mg. Bottles of 40, 100 and 500.
INJECTION 25 mg. per ml. Vials of 10 ml.
EYE DROPS 1% Bottles of 3 ml.
EYE OINTMENT 1% Tubes of 3 G.

HYDROCORTISTAB (HYDROCORTISONE)

TABLETS 20 mg. Bottles of 100.
INJECTION (Intravenous) 5 mg. per ml. for intravenous injection after dilution. Ampoules of 20 ml.

INJECTION (local) 25 mg. per ml. Hydrocortisone acetate suspension. Vials of 5 ml.
OINTMENT 1% Tubes of 5 G. and 15 G.
OINTMENT 2.5% Tubes of 5 G. and 15 G.
EYE DROPS 1% Bottles of 3 ml.
EYE OINTMENT 2.5% Tubes of 3 G.



Further details will be gladly sent on request to
BOOTS PURE DRUG CO. LTD. NOTTINGHAM, ENGLAND

3246

A new compound

(4,4'-diacetoxy-diphenyl)-(pyridyl-2)-methane

Dulcolax

Regd. Trade Mark

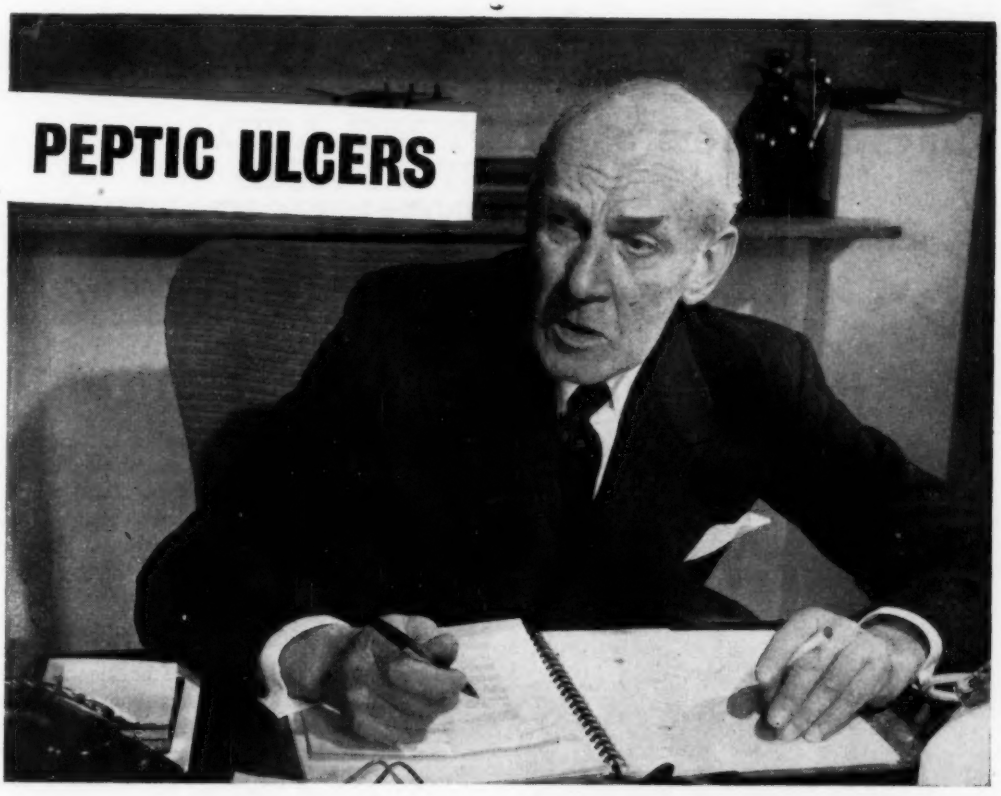
Contact Laxative free from systemic effects

Enteric Coated Tablets
act overnight

Suppositories
promptly empty the lower bowel
replacing the enema

Supplied Tablets (enteric coated) of 0.005 g.
Bottles of 30 and 200
Suppositories of 0.01 g. Boxes of 6 and 50

LEWIS LABORATORIES LTD., LEEDS 9



Pursuing his normal (pH) business

Benjamin McDougall, Esq., is a typical hard-pressed businessman. Year after year he carries a heavy burden of worrying responsibility. Peptic ulcers trouble him at intervals and the threat of them is always present.

A clear case for ALUPHOS TABLETS Aluphos Tablets, alone of common antacids, buffer the gastric secretion to pH 2.0—2.5—a normal value at which peptic digestion is not inhibited.

As a buffer, Aluphos Tablets act quickly and remain effective for several hours. Aluphos Tablets cannot cause 'acid rebound' and there is no risk of alkalosis. They are non-constipating. Mr. McDougall will appreciate Aluphos Tablets because they are palatable, portable and efficient.

Aluphos Tablets are economical—the basic N.H.S. price is 2/7d. per box of 50 tablets.

A clear case for ALUPHOS TABLETS

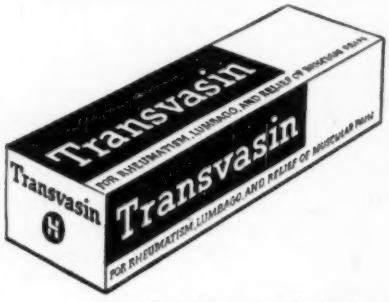
BENGER LABORATORIES LIMITED · HOLMES CHAPEL · CHESHIRE

A BENGER PRODUCT

Transvasin

brings the esters of NICOTINIC ACID SALICYLIC ACID p-AMINOBENZOIC ACID to the focal point of soft-tissue rheumatism

The esters in Transvasin, a new preparation developed by Hamol S.A., our Swiss associates,* readily pass the skin barrier in therapeutic quantities and enable an effective concentration of the drugs to be built up where they are needed.* Transvasin not only induces vasodilation of the skin with a superficial erythema, but also brings about a deep hyperaemia of the underlying tissues. It is non-irritant, and can be safely used on delicate skins. It is now being widely prescribed with successful clinical results. Since a very small quantity is sufficient for each application, the cost of treatment is extremely low.



Salicylic acid tetrahydrofurfuryl-ester	14%
Nicotinic acid ethyl-ester	2%
Nicotinic acid n-hexyl-ester	2%
p-Aminobenzoic acid ethyl-ester	2%
Water-miscible cream base ad	100%

**Therapeutische Umschau VIII*, 1952, 10, 143

Transvasin is available in 1 oz. tubes, basic price 2/6 plus 9d. P.T., and is not advertised to the public. Samples and literature will be gladly sent on application.

LLOYD-HAMOL LTD., 11 WATERLOO PLACE, LONDON, S.W.1. WHITEHALL 8654/5/6

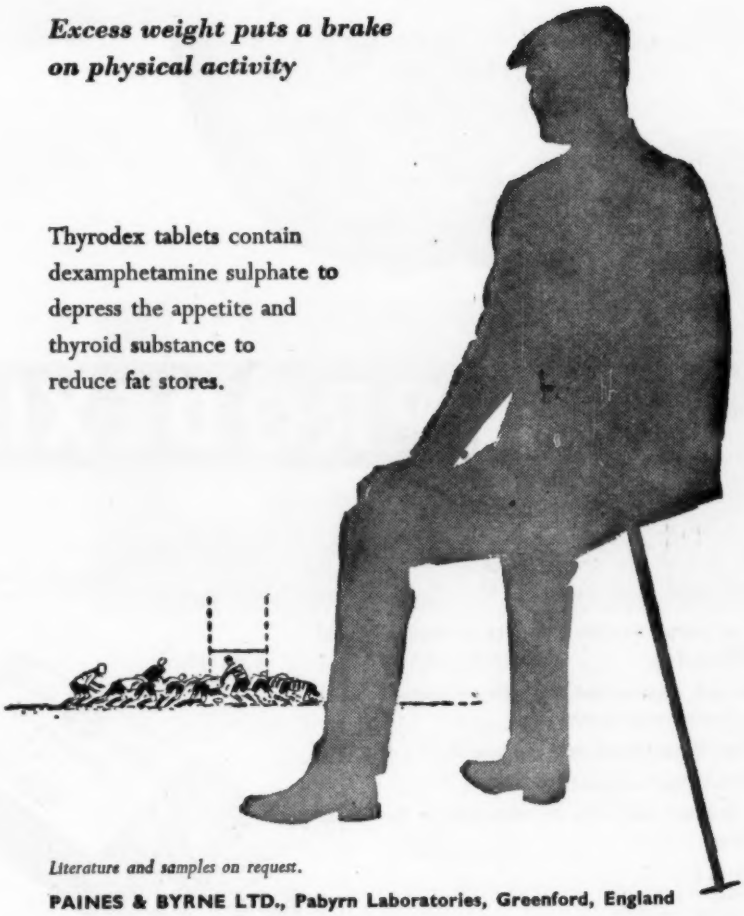
Transvasin is the registered trade mark of Lloyd-Hamol Ltd.

A well-proved formula

THYRODEX

TABLETS

Excess weight puts a brake on physical activity



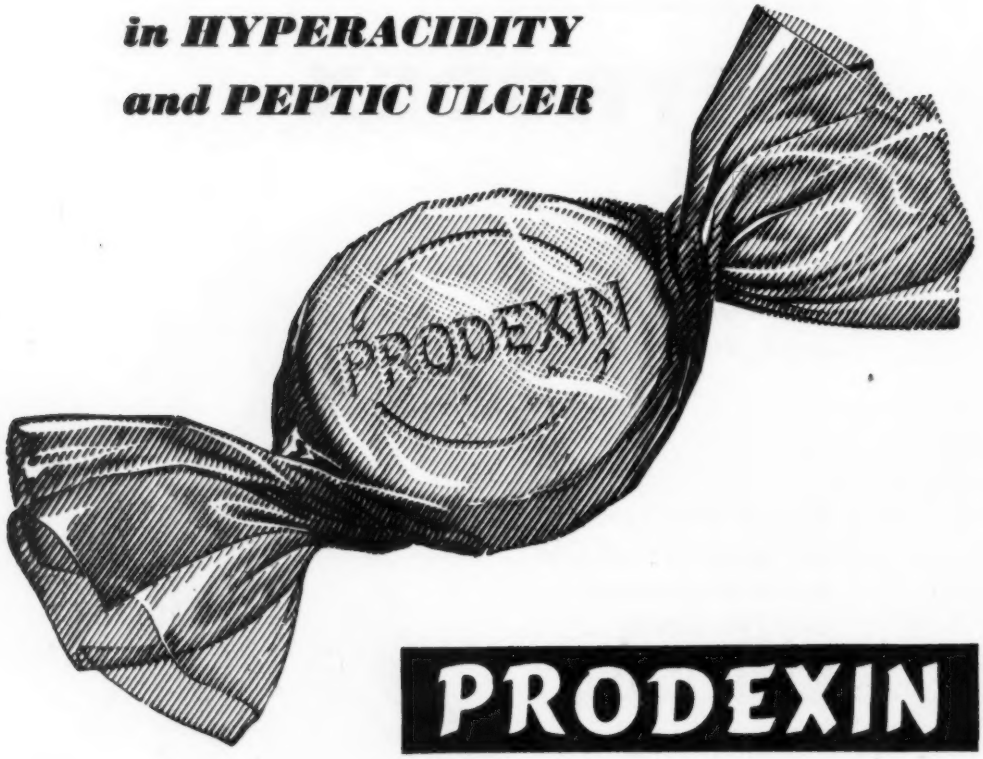
Thyrodex tablets contain dexamphetamine sulphate **to** depress the appetite and thyroid substance to reduce fat stores.

Literature and samples on request.

PAINES & BYRNE LTD., Pabyrn Laboratories, Greenford, England

For True Buffer Action...

in HYPERACIDITY and PEPTIC ULCER



PRODEXIN

Prodexin has all the attributes of a true buffer, and more besides:

- it keeps gastric acidity down to an equable level (*p*H 3·5 to 4·5).
- it does not alkalise the stomach contents, so that acid rebound cannot occur.
- its effect is consistent and prolonged.
- it does not vary in potency.
- it is pleasant and safe to take and is free from grittiness.

FORMULA

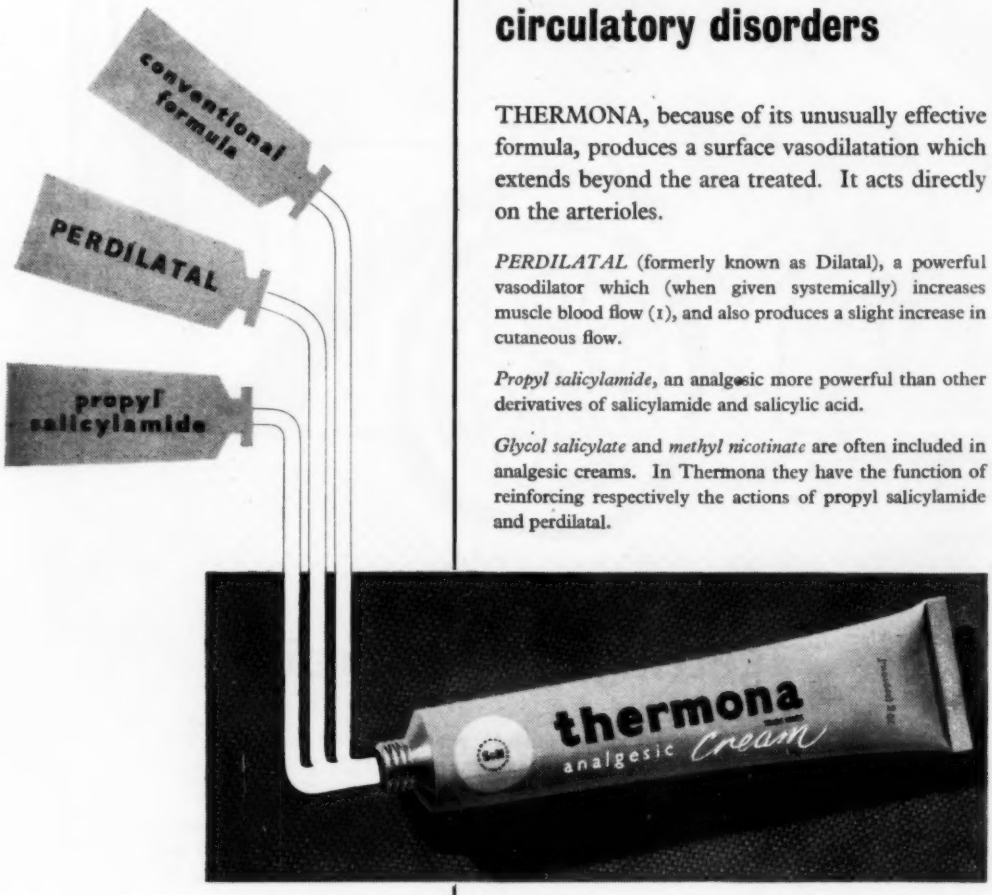
Aluminium glycinate	0·9 gm
Magnesium carbonate	0·1 gm

Reference: *Practitioner*, 173: 46, 1954.

PACKAGES
Cartons of 30 individually wrapped tablets.
Dispensing packs of 240 tablets.

C. L. BENCARD LTD. PARK ROYAL LONDON, N.W.10

Vasodilator relief of rheumatic pain and local circulatory disorders



THERMONA, because of its unusually effective formula, produces a surface vasodilatation which extends beyond the area treated. It acts directly on the arterioles.

PERDILATAL (formerly known as Dilatal), a powerful vasodilator which (when given systemically) increases muscle blood flow (1), and also produces a slight increase in cutaneous flow.

Propyl salicylamide, an analgesic more powerful than other derivatives of salicylamide and salicylic acid.

Glycol salicylate and *methyl nicotinate* are often included in analgesic creams. In Thermona they have the function of reinforcing respectively the actions of propyl salicylamide and perdilatal.

FORMULA

PERDILATAL 1-(p-hydroxyphenyl)-2-(1'methyl-3'-phenyl-propylamino)-propanol-(1) hydrochloride	0.3%
Propyl salicylamide	5.0%
Methyl nicotinate	1.0%
Glycol salicylate	10.0%
Vanishing cream base	83.7%

(1) *Lancet*, 1956, *i*, 257.

INDICATIONS

(1) The group of conditions covered by the terms 'muscular rheumatism' and 'fibrositis'.

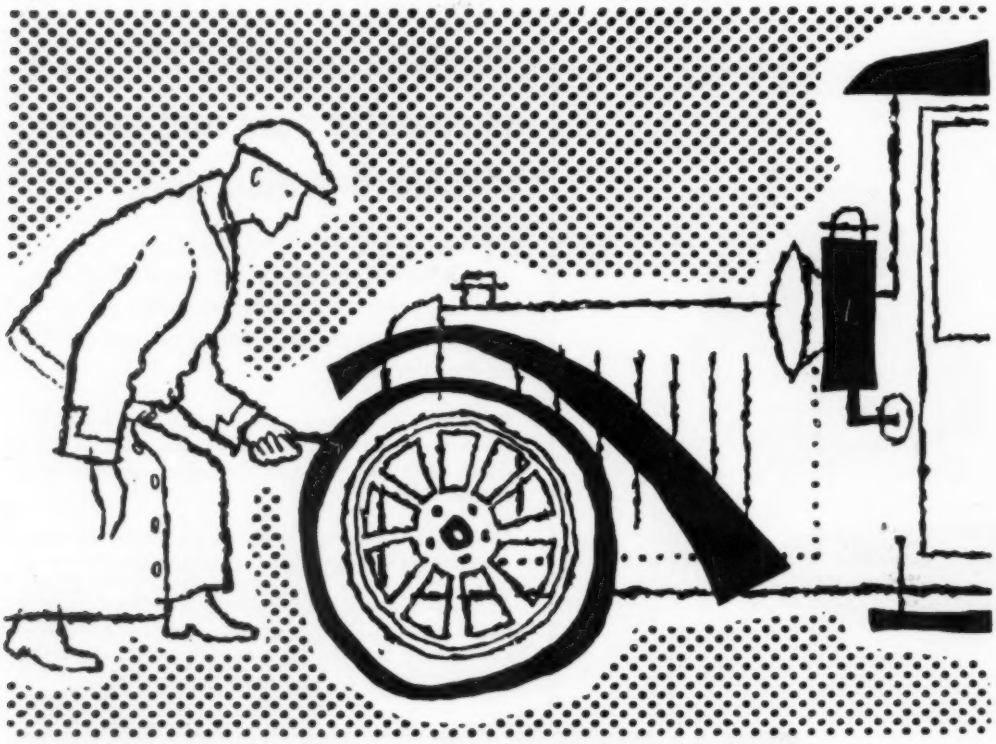
(2) Local circulatory disorders where they have surface manifestations (e.g., chilblains, Raynaud's disease)

AVAILABILITY

Tubes containing 20 G (approx.) prescribable on N.H.S. form E.C.10.

an S&N product

SMITH & NEPHEW LTD · WELWYN GARDEN CITY · HERTS



getting started again

Two features of the common "bilious" attack are biliary stasis and constipation. Rational therapy should attack both aspects of the condition, permitting the normal process of digestion to start again.

Veracolate cholagogue-evacuant does this by combining bile salts therapy with a mild purgative action. The bile salts stimulate the production and flow of bile, while the cascara and phenolphthalein assist evacuation of the intestinal tract.

Active principles: Sodium taurocholate and glycocholate, 1.07 gr., ext. cascara sagrada. 1.00 gr., phenolphthalein 0.50 gr., oleoresin capsicum 0.04 gr.

Dose: One tablet 3 times a day or 2 at night, with water.

Packing: In bottles of 50 and 100 tablets. Bottles of 500 tablets supplied to chemists for dispensing.

Veracolate

No Warner preparation has ever been advertised to the public.

WILLIAM R. WARNER & CO. LTD., POWER ROAD, LONDON, W.4.

an all-round defence against

in all its phases

The relief of pain is rightly the patient's just insistence. Effective alleviation may be obtained in many pain producing conditions which increase seasonally. Rheumatism, lumbago, arthritis, coryzal and influenzal aches are but some of the common ailments which call for a rapid form of therapy. Hypon Tablets fulfil the requirements of a safe analgesic without any untoward side effects being experienced. Caffeine and phenolphthalein present in Hypon Tablets ensures a preparation which is the best in its category

FORMULA: *Acid Acetylsalicyl B.P. 40.22% Phenacet. B.P. 48.00% Caffein B.P. 2.00% Codein. Pnosph. B.P. 0.99% Phenolphthal. B.P. 1.04% Excip. 7.75% (each tablet 8 grains)*

HYPON TABLETS

Prescribe Hypon Tablets by name

CALMIC LIMITED, CREWE. *Phone CREWE 3251-5* **LONDON:** *2 Mansfield St., W.1. Phone LANgham 8032-9*

AUSTRALIA: 458-468 Wattle Street, Ultimo, Sydney, N.S.W.

CANADA: Terminal Buildings, York St., Toronto.

H2

BAYER

A NEW Development in analgesics

Panadol (N-acetyl-p-aminophenol) is a potent analgesic and antipyretic, new to this country. Clinical trials have shown it to be much better tolerated than Tab. Codein. Co. Panadol is therefore a valuable alternative to currently-used analgesics in arthritic, muscular and neuralgic pain, headaches and colds.

NO ASPIRIN—*no gastric irritation*
NO PHENACETIN—*no methaemoglobinaemia*
NO CODEINE—*no constipation*

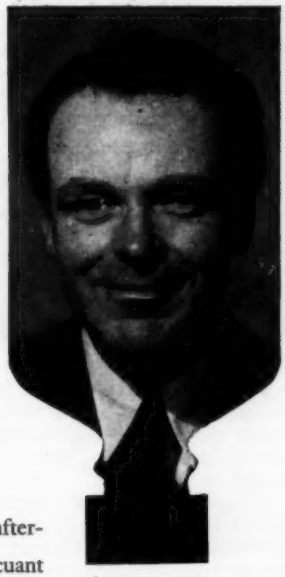
PANADOL
Trade Mark

Packings: tablets, 0.5 g., in bottles of 100 and 500. The basic N.H.S. cost of 24 tablets is 1/11½d. Dosage: 1-2 tablets, generally not more than eight in one day.
A sample and Medical literature gladly sent on request.

BAYER PRODUCTS LIMITED

NEVILLE HOUSE · KINGSTON-ON-THAMES · SURREY

Associated export company: WINTHROP PRODUCTS LIMITED.



the 'family' tree . . .

A species of buckthorn tree supplies the 'sacred bark' from which Cascara Evacuant is made. Introduced to medicine by Parke, Davis over 50 years ago it is the ideal laxative for the safe and gentle relief of occasional or chronic constipation . . . for people of every age, in every family. A refined and palatable liquid; non-griping, non-habit forming, with no great tendency to after-constipation, Cascara Evacuant can be used for years without ill-effect. It is a *natural* tonic laxative.

Cascara Evacuant

PARKE-DAVIS

THE IDEAL TONIC LAXATIVE

Parke, Davis & Company Limited, *(inc. U.S.A.)* Hounslow, Middlesex. Tel: Hounslow 2361

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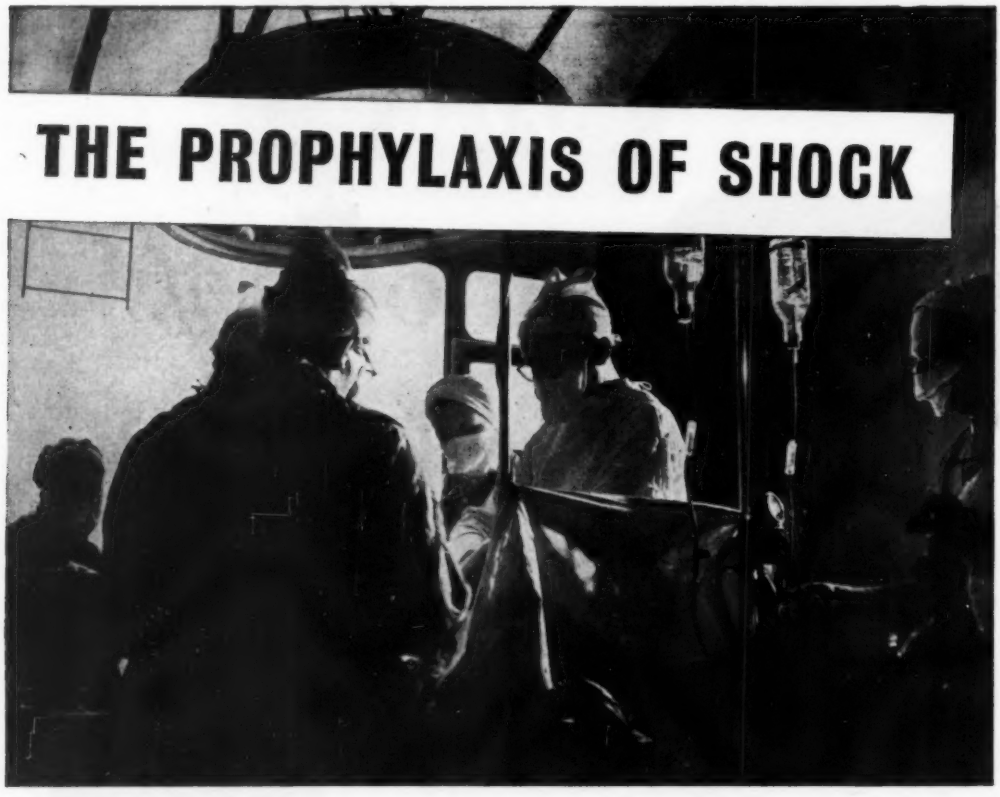


THE PROPHYLAXIS OF SHOCK

A MAJOR OPERATION is in progress. It is essential that the patient's circulating blood volume be maintained—especially during the following critical twenty-four hours.

A CLEAR CASE FOR DEXTRAVEN, the established clinical dextran solution. Dextraven is eminently suitable for the prophylaxis of surgical shock. Also for immediate treatment following trauma. Raising the blood pressure swiftly and surely, it stays in the circulation in significant concentration during the vital post-operative twenty-four hours.

DEXTRAVEN CAN BE given immediately by intravenous infusion. Stable indefinitely under all conditions, it requires no special storage precautions.

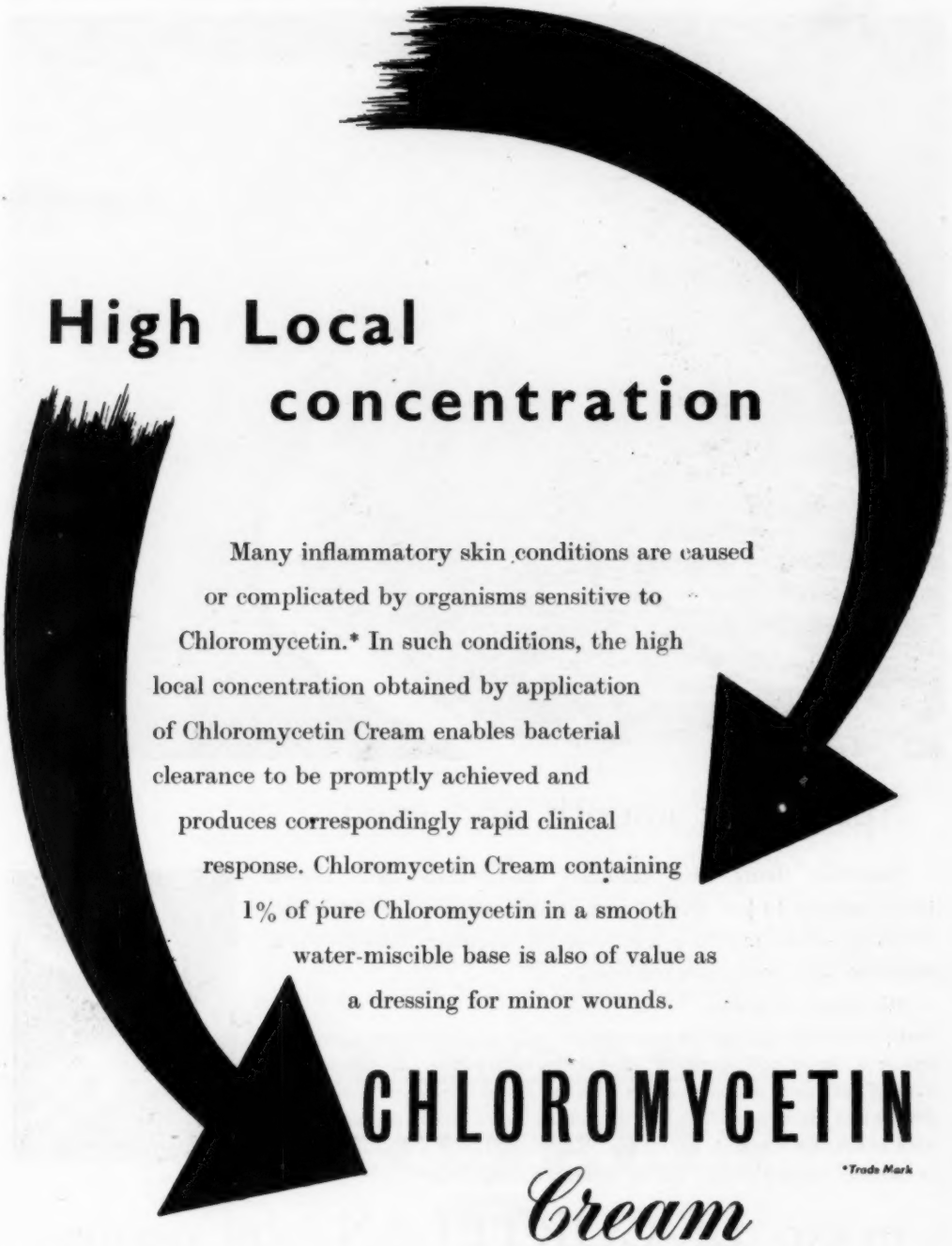
DEXTRAVEN IS APPROVED by the Ministry of Health. Fully descriptive literature is available and a Technical Information Service is always at your disposal.

A clear case for **DEXTRAVEN** TRADE MARK

BENGER LABORATORIES LIMITED · HOLMES CHAPEL · CHESHIRE

A BENGER PRODUCT

D.5 (REV. 2)



High Local concentration

Many inflammatory skin conditions are caused or complicated by organisms sensitive to Chloromycetin.* In such conditions, the high local concentration obtained by application of Chloromycetin Cream enables bacterial clearance to be promptly achieved and produces correspondingly rapid clinical response. Chloromycetin Cream containing 1% of pure Chloromycetin in a smooth water-miscible base is also of value as a dressing for minor wounds.

CHLOROMYCETIN

*Trade Mark

Cream

Packed in collapsible 1-oz. tubes

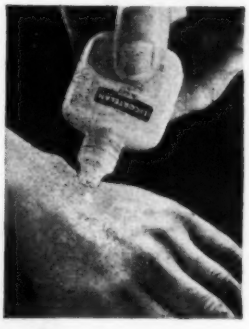
MEDICAMENTA VERA

PARKE, DAVIS & Company, Ltd. *(Inc. U.S A.)* Hounslow, Middlesex, Tel: Hounslow 2361

223

Spreading smooth and even . . .

Smoothly, thinly and painlessly Ef-Cortelan Skin Lotion (hydrocortisone Glaxo) spreads over tender surfaces. Swiftly, safely, effectively—sometimes in a few hours—it suppresses inflammation, exudation and allergic skin reactions.



A little goes a long way.

Most conditions are adequately controlled by the 0.5% Ef-Cortelan Lotion and, because it has superior spreading and penetrating qualities and brings hydrocortisone into more intimate contact with the tissues, the lower strength is as effective as a 1% ointment. This, and the fact that only a little of the lotion is used, offers appreciable economic advantages. Ef-Cortelan Lotion is especially suitable for extensive, weeping surfaces and for application to the scalp.

GLAXO EF-CORTELAN SKIN LOTION

(0.5% and 1% hydrocortisone alcohol in water-miscible base) in 20 cc. squeeze bottles.

ALSO FROM THE GLAXO CORTISONE RANGE. EF-CORTELAN SKIN OINTMENT NO. 1 (1% and 2½% hydrocortisone acetate in *non-greasy* base); EF-CORTELAN SKIN OINTMENT NO. 2 (1% and 2½% hydrocortisone acetate in *greasy* base). Both in 5 g. and 15 g. tubes; 50 g. jars.

GLAXO LABORATORIES LTD., GREENFORD, MIDDLESEX BYRon 3434

Clearing the site
for quicker healing

Prompt disposal of pus and clotted blood is an all-important step in the successful treatment of infected lesions and wounds. Until these barriers are removed, adequate drainage may be impossible, access denied to antibiotic medication and the natural defences may be seriously hampered. VARIDASE breaks down such barriers by dissolving pus and blood clots through enzymatic action. Apart from its many applications in surgical procedures, VARIDASE is a weapon of immeasurable value in day-to-day practice—as a dressing for varicose ulcers, suppurating wounds, infected burns and other topical lesions. When VARIDASE is used with C.M.C. (Carboxymethylcellulose) Jelly, enzymatic action is maintained for up to 24 hours and the need for wet dressings is eliminated.

VARIDASE* *with* C.M.C. JELLY

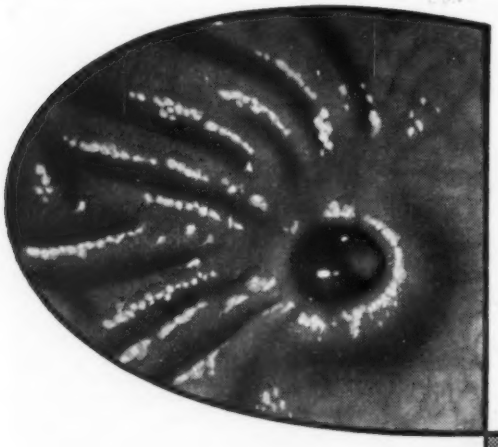
Lederle

Varidase is issued in vials (25,000 units) containing Streptokinase 20,000 units and Streptodornase, 5,000 units; vials (125,000 units) containing Streptokinase 100,000 units and Streptodornase 25,000 units. C.M.C. Jelly 4.5%, jars of 15 cc.

* Regd. Trade-Mark

LEDERLE LABORATORIES DIVISION

Cyanamid PRODUCTS LTD. LONDON, W.C.2



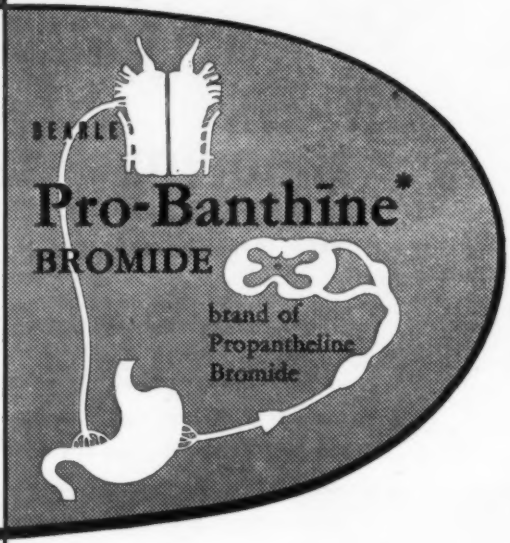
The safe

anticholinergic agent

for

Peptic Ulceration

A large number of cases of peptic ulceration have been successfully treated with "Pro-Banthine". By its anticholinergic action inhibiting transmission of neural stimuli at both sympathetic and parasympathetic ganglia and at parasympathetic myoneural junctions, hypermotility of the stomach and duodenum is reduced. This results in rapid relief of pain. "Pro-Banthine" is easily administered, orally. It has few side-effects, which are all readily eliminated by adjustment of dosage.



"Pro-Banthine" is also available as a compound tablet with Phenobarbitone. It is especially indicated when peptic ulceration is complicated by mental stress, anxiety, and nervousness. Dosage of both forms is usually 15 to 30 mg. (1 or 2 tablets) four times daily. "Pro-Banthine" is available in bottles of 40, 100, and 1,000 tablets, each tablet containing 15 mg. of Propantheline Bromide, and compounded with Phenobarbitone (15 mg.) in bottles of 100 and 1,000 tablets.

Literature on request

*REGISTERED TRADE MARK

SEARLE

G.D. SEARLE & CO., LTD.

83, Crawford Street

London, W.1

Telephone: Paddington 4034

Symbol of security

To physician and patient alike, ACHROMYCIN tetracycline affords a very real sense of *security* in antibiotic therapy. From the physician's viewpoint, ACHROMYCIN gives added assurance of swift response in a broad range of infections—paving the way to rapid, uneventful recovery. To the patient, ACHROMYCIN offers a treatment of greater comfort and simplicity . . . a treatment that is quick to win his co-operation and confidence. Here then is true security—in every sense.

ACHROMYCIN*

TETRACYCLINE

unsurpassed for versatility . . . potency . . . economy

Available in the following forms:

CAPSULES · EAR SOLUTION · INTRAMUSCULAR
INTRAVENOUS · OINTMENT · OPHTHALMIC
OINTMENT · OPHTHALMIC POWDER STERILIZED
ORAL SUSPENSION · PEDIATRIC DROPS · SOLUBLE
TABLETS · SPERSOIDS* Dispersible Powder · SYRUP
TABLETS · TROCHES

ACHROMYCIN · LYNN BROAD · antibiotic

*Regd. Trade-Mark

50 Lederle FIFTIETH ANNIVERSARY

LEDERLE LABORATORIES DIVISION

Cyanamid PRODUCTS LTD. LONDON, W.C.2

At last—fully active by mouth

PENICILLIN-V, LILLY

SUITABLE FOR ALL AGE GROUPS

PENICILLIN-V, LILLY is a completely new penicillin for oral use. Stable in the presence of gastric secretions, PENICILLIN-V gives higher and more prolonged blood levels than any other oral penicillin. It is therapeutically comparable with parenteral penicillin ; high and wasteful dosage is unnecessary.

'PULVULES' PENICILLIN-V, LILLY, each containing 125 mg.—in bottles of 12 and 100. Average adult dose—1 capsule three times daily, increased in severe infections.

SUSPENSION PENICILLIN-V LILLY, PAEDIATRIC contains 62.5 mg. in each large teaspoonful. in bottles to make 60 c.c. Pleasantly flavoured Average dose for children—one teaspoonful three or four times daily.

Lilly TRADE MARK

ELI LILLY & COMPANY LIMITED

BASINGSTOKE HANTS

A NEW ORAL CHEMOTHERAPEUTIC FOR TUBERCULOSIS

A new chemical compound formed by the combination of INH and PAS in molecular proportions

DIPASIC IS AVAILABLE FOR INVESTIGATION

LITERATURE ON THERAPY AND DOSAGE ON REQUEST

DIPASIC

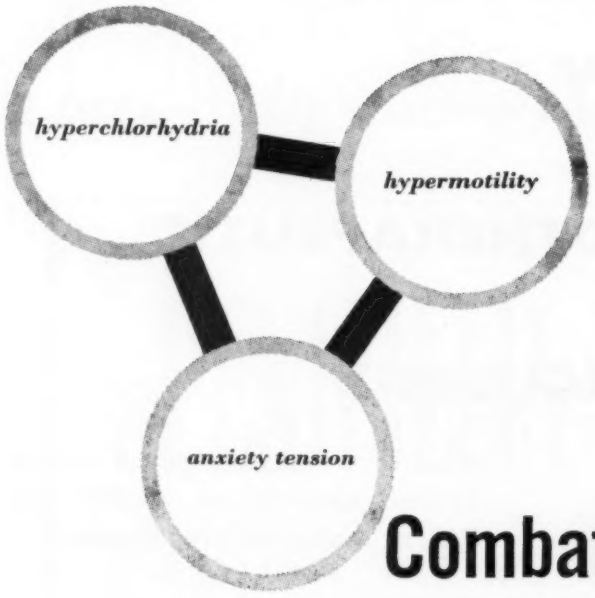
TABLETS OF 100 mg. OF ISONICOTINIC ACID HYDRAZIDE-P-AMINOSALICYLATE

GEWO

BENGUE & CO. LTD. *MANUFACTURING CHEMISTS*

MOUNT PLEASANT - ALPERTON - WEMBLEY - MIDDLESEX

BENGUE & CO. LTD. MAKE "DIPASIC" AVAILABLE IN THE UNITED KINGDOM BY ARRANGEMENT WITH ED. GEISTLICH SONS LTD., WOLHUSEN (SWITZERLAND).



Combat the peptic ulcer triad with *Collubarb* tablets

Each active constituent in COLLUBARB has a specific function in the treatment of dyspepsia, hyperacidity and peptic ulceration, and provides effective symptomatic relief.

HYPERCHLORHYDRIA	Aluminium Hydroxide 5 gr. (320 mg.)
ANXIETY TENSION	Phenobarbitone ¼ gr. (16 mg.)
HYPERMOTILITY	Atropine Sulphate 1/500 gr. (0.13 mg.)
Presentation	Cartons of 24 and 100 (film wrapped) Containers of 500

EVANS MEDICAL

EVANS MEDICAL SUPPLIES LTD, LIVERPOOL & LONDON

600

INTRODUCING THE ORIGINAL BRAND

OF BUTHALITONE SODIUM*

'ULBREVAL'

TRADE MARK

the ultra-brief-acting intravenous anæsthetic

Ulbreval is of outstanding value in all procedures and on all occasions when a rapid return of the patient to a normal level of consciousness is both time-saving and convenient.

SUPPLIES

Boxes of 5 x 1 G. ampoules.

Boxes of 25 x 1 G. ampoules.

* Sodium 5-allyl-5-*iso*butylthiobarbiturate

Manufactured by

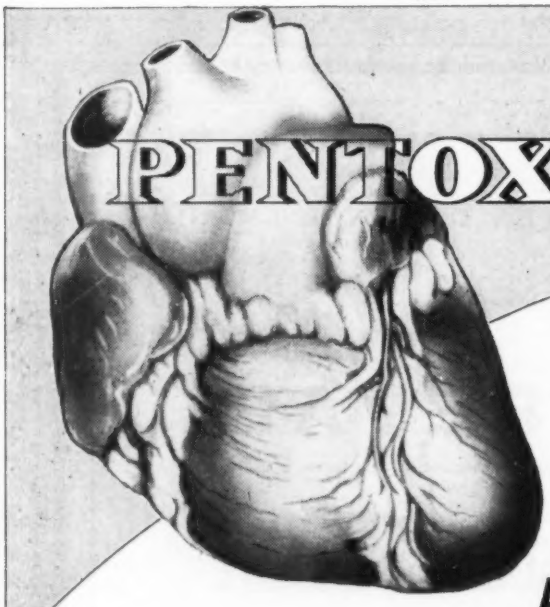
FARBENFABRIKEN BAYER A.G.

LEVERKUSEN

Sole Distributors in the U.K.

JOHN WYETH & BROTHER LIMITED

CLIFTON HOUSE, EUSTON ROAD, LONDON, N.W.1



PENTOXYLON

... the new therapy

for

Angina Pectoris

In 'Pentoxylon' the tranquillizing, bradycardic influence of 'Rauwiloid' brand alkaloid hydrochlorides of Rauwolfia serpentina is allied to the prolonged vasodilating effect of pentaerythrityl tetranitrate. This new combined therapy represents an important advance in the long term treatment of angina pectoris.

Although some patients will still occasionally require glyceryl trinitrate, in many others 'Pentoxylon' will provide complete relief from anginal attacks. It will also bring: "*gratifying reduction of anxiety and relief of apprehension . . .*"

North-West Med. (1955) 54: 34

Dose: 1 tablet four times a day, before meals, increased later if necessary.

RIKER

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Owing to its wide range of antibacterial activity, Chloromycetin "is the drug of choice in the treatment of laryngotracheobronchitis" . . . in which "the infecting organisms are either penicillin-insensitive or usually penicillin-resistant."

Med. Press 233:485, 1955

Septic Abortion May, 1955

In a review of 995 cases of septic abortion treated in a special puerperal sepsis unit, a number of cases were due to infection with coliform organisms or penicillin-resistant staphylococci. "Since 1951" state the authors "we have been impressed with the efficacy of Chloromycetin in this type of case."

Brit. med. J. 2:1239, 1955

Staphylococcal Empyema July, 1955

12 of 13 cases of penicillin-resistant staphylococcal pneumonia in infants and children, complicated by lung abscess and empyema, responded dramatically to Chloromycetin—"the most effective drug". Chloromycetin was indicated by *in vitro* sensitivity tests in all cases in this series.

Canad. M.A.J. 73:787, 1955

Acute Pyelonephritis in the Diabetic September, 1955

In a "condition which in most cases would otherwise be fatal", it is desirable to use an antimicrobial agent likely to be effective against the common urinary pathogens as well as organisms liable to produce secondary infection. "Chloromycetin offers the best chance of success and it is more likely to clear the infection with the first intensive course of treatment."

Canad. M.A.J. 73:956, 1955

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EFFECTS OF FEEDING DIFFERENT FATS ON SERUM-CHOLESTEROL LEVEL

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A SURVEY of the multiracial community residing in the Cape Peninsula revealed that the widely differing inter-racial incidence of coronary heart-disease was associated with a parallel difference in the mean serum-cholesterol levels (Bronte-Stewart et al. 1955a). Within each racial group the serum-cholesterol level was highest in those on the highest economic plane and bore a parallel relationship to the intake of foods rich in fat of animal origin. There was no correlation with the intake of vegetable fat. Diets which through economic privilege have increasing quantities of foods containing animal fat also have increasing quantities of animal proteins, with resulting changes in the intake of vitamins, and decreasing quantities of starch and cellulose. It became necessary, therefore, to study the effect of various foodstuffs on the serum-cholesterol level under controlled conditions.

Material

This study was conducted on two groups of people: 6 volunteers with initial low-serum-cholesterol levels and accustomed to a low-fat diet (about 17% of calories from fat); and 2 patients with initial high serum-cholesterol levels and accustomed to a diet rich in animal fat. The 2 patients, who agreed to coöperate in the investigation, were European males, aged 38 and 42, with angina pectoris and electrocardiographic evidence of coronary heart-disease. The 6 volunteers were 5 Bantu males and 1 Cape Coloured male from the poorer economic strata. With 1 exception, no abnormal physical signs were observed in the volunteers during the study. 4 had been admitted with vitamin-deficiency syndromes and had received vitamin therapy before the start of this study, and these vitamin supplements were continued throughout. The 1 exception was studied during physiotherapeutic rehabilitation after hemiplegia, probably syphilitic. Physical activity was minimal throughout the study.

Diets Used

Throughout the study the 2 Europeans with coronary heart-disease were kept on a constant diet containing a moderate amount of fat (50 g. daily) almost exclusively of animal origin in the form of butter, milk, and meat. The basic diet of the 6 non-European volunteers consisted of maize-meal products and white bread supplemented by sugar and casein to maintain by suitable adjustment an isocaloric and isonitrogenous state. This diet is free from cholesterol, and the small amount of fat present is that contained in the maize and bread, estimated to be not more than 3% of the total calories (Fox and Golberg 1944). The first 2 non-Europeans were studied without casein supplements and were maintained on a protein-poor diet (28 g. daily) throughout by the use of finely sifted maize meal (baker's cones). In another volunteer the intake of protein was deliberately altered by changing from baker's cones to standard maize meal (an increase of about 7 g. of protein daily) and later supplementation of this daily intake of protein with 100 g. of casein.

To these diets various fats and oils were added one at a time, usually in amounts of 100 g., to increase the proportion of calories derived from fat from the basic 3% to 36% and 45% and, on occasion, to 60–70% (200 g.). With this sudden increase in intake of fat transient diarrhœa developed on two occasions but ceased spontaneously without reduction of the intake of fat. The oils were administered either as a draught or incorporated in the food, according to individual preference. When the oils were given in cooked food, this was fried at moderate or low temperatures. In view of Page's (1954) warning that there may be an individual variation in the response to fat feeding, our policy was to try several different fats on the same person.

Methods

Blood was drawn every other day with the subject fasting, and the cholesterol was estimated in duplicate firstly in the fresh sera and secondly on filter-paper containing the electrophoretically separated lipoproteins by the method of Abell et al. (1952) modified by Anderson and Keys (1955) as in the previous survey (Bronte-Stewart et al. 1955a). Cholesterol in stools was estimated by the same method.

With this method, storage of the frozen sera did not affect the cholesterol values. Use was made of this to cross-check the trends that evolved by re-estimating a specimen of serum from the previous week. By these methods the same fat given three months later to the same volunteer produced almost identical serum-cholesterol levels (figs. 2 and 6).

Isolation of Fatty-acid Fractions

Two fatty-acid fractions were separated from sunflower-seed oil by fractional crystallisation from acetone

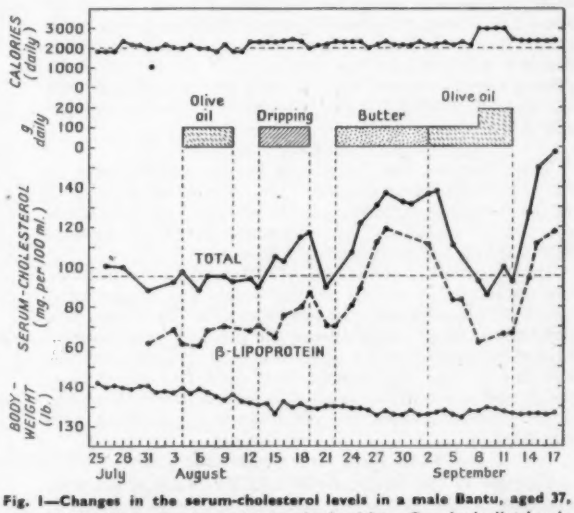

Fig. 1—Changes in the serum-cholesterol levels in a male Bantu, aged 37, coincided with changes in the intake of animal fat. On a basic diet low in protein and fat and free from cholesterol a supplement of olive oil did not raise the serum-cholesterol level or maintain the raised level when substituted for butter. Even when the olive-oil supplement was doubled so that it provided over 60% of the total calories, the serum-cholesterol level did not rise again until a "full diet" consisting of beef and vegetables (fat-content about 140 g.) was given. The mean serum-cholesterol level before fat feeding was 95·6 ± 5·5 mg. per 100 ml.

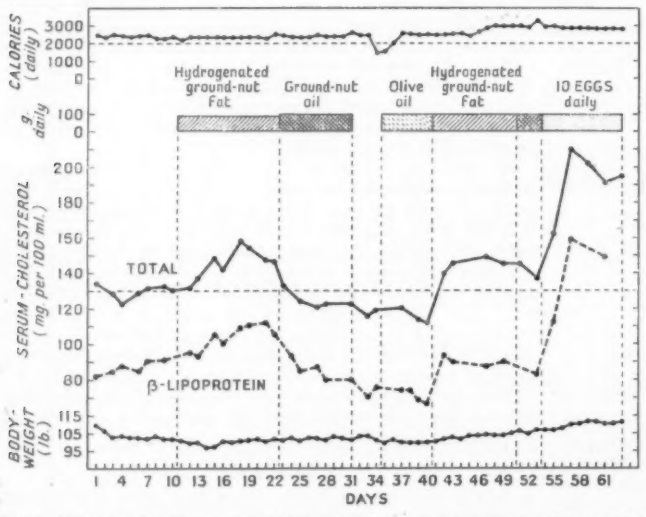

Fig. 2—A slight rise in the serum-cholesterol level of a male Bantu, aged 65, coincided with the feeding of hydrogenated ground-nut fat. On switching to the natural oil the changes were reversed. On re-feeding with hydrogenated fat the serum-cholesterol level rose again. The amount of the rise was slight compared with that from an equivalent amount of fat as eggs. The mean serum-cholesterol level before the fat feeding was 129·6 ±3·5 mg. per 100 ml.

at low temperatures (Markley 1947). The saturated fraction, a palmitate-stearate mixture, was removed at −20°C, and the temperature was lowered successively to −50°C and −70°C to separate off the oleic and linoleic fractions respectively. Subsequently the saturated fraction and the most highly unsaturated fraction so obtained were esterified with ethyl alcohol, followed by fractional distillation in a high vacuum.

The unsaturated fraction contained no sterol, determined by the Liebermann Burchard reaction by the method of Abell et al. (1952). The iodine values (140–150) indicated that in using this method of fractionation we could not obtain a linoleate fraction completely free from other less unsaturated fatty acids. The vitamin-E content, measured by the method of Quackenbush et al. (1941), never exceeded that present in the sunflower-seed oil and in most instances was far less (18–70 mg. per 100 g.).

Results

The effects of the short-term feeding experiments on the serum-cholesterol levels are shown in figs. 1–7, which show that differences in the serum-cholesterol levels are usually paralleled by differences in the cholesterol contained in the β-lipoprotein fraction.

Investigation of the effects of different fat fractions on the excretion of sterols in the stools are in progress. Some results are shown in figs. 6 and 7. In 1 case (not illustrated) fæcal sterol during the period of administration of hydrogenated fat alone was 0·39 g. daily, with the addition of the unsaturated fatty-acid fraction 0·83 g. daily, and after withdrawal of both supplements 0·53 g. daily. These values are insufficient for drawing firm conclusions.

ANIMAL FATS AND VEGETABLE OILS

Changes in the serum-cholesterol levels coincided with changes in the intake of fat. In the first 2 cases it appeared that the findings of the inter-racial survey had been confirmed, in that olive oil, representing a vegetable oil, had no effect, whereas butter and beef dripping (tallow) in equivalent amounts and beef muscle promptly raised the serum-cholesterol level (fig. 1). Olive oil substituted for the butter or tallow could not maintain the raised level, which remained low even when the olive-oil supplement was doubled so that more than 60% of the total calories was provided by this oil.

A hardened or hydrogenated ground-nut fat was tried (iodine value 55). In the first case studied there was a slight but prompt rise of the serum-cholesterol level. When the non-hydrogenated natural oil (iodine value 89) was substituted, the serum-cholesterol level fell (fig. 2). The same effects were seen later in the same person and in 2 others. This effect of hydrogenation influenced the design of subsequent experiments.

Sunflower-seed oil was fed in the presence of high serum-cholesterol levels. In the post-hemiplegic patient the serum-cholesterol level rose on the administration of 100 g. of beef dripping. When the intake of fat was raised to 200 g. with 100 g. of sunflower-seed oil (iodine value 135), the serum-cholesterol levels fell, only to rise again when the sunflower-seed oil was withheld (fig. 3). In the same volunteer the effect of ten boiled eggs was reversed when the eggs were scrambled or fried in 100 g. of sunflower-seed oil. After a control period on 50 g. of animal fat the intake of fat in the 2 European volunteers with coronary heart-disease was increased to 150 g. by the addition of 100 g. of sunflower-seed oil. Immediately the serum-cholesterol levels fell (fig. 4). When the sunflower-seed oil was withheld and the total intake of fat thereby decreased, the serum-cholesterol level returned to its original value. The experiment was repeated in 1 of these 2 volunteers with 100 g. of ground-nut oil, which produced a similar but smaller effect.

Marine Oils

Neither pilchards fried in pilchard oil (iodine value 180) nor seal oil (iodine value 166) raised the serum-cholesterol levels in 3 volunteers. On the contrary, the level attained during the feeding of these oils was lower than that on the fat-free basic diet (fig. 5). The effect of the highly unsaturated fraction segregated from pilchard

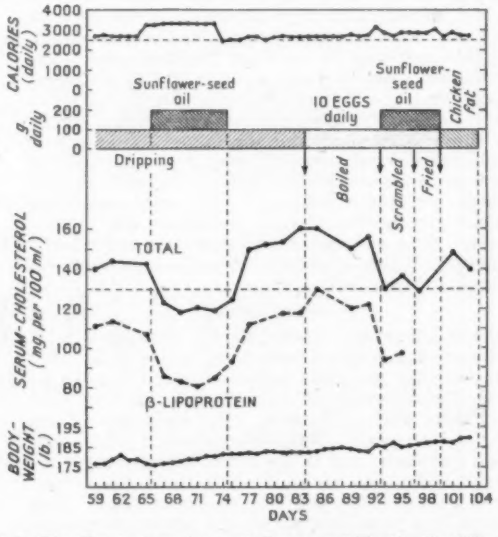

Fig. 3—The effect is shown in a male Bantu, aged 37, of feeding 100 g. of animal fat daily followed by an increase of the total intake of fat to 200 g. by feeding equal quantities of an animal fat and a vegetable oil. The egg ration was given first as ten boiled eggs daily followed by ten eggs scrambled or fried in sunflower-seed oil.

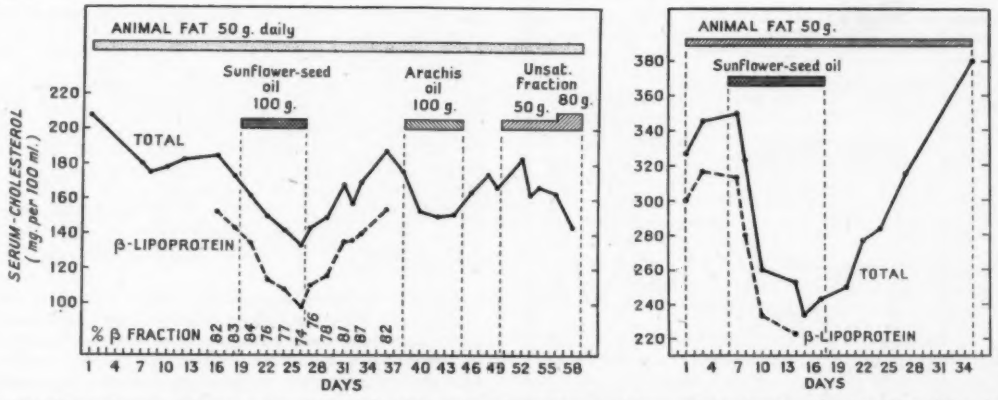

Fig. 4—The effect is shown, in 2 Europeans, aged 38 and 42, with coronary heart-disease, of increasing the intake of fat from 50 to 150 g. daily by the addition of 100 g. of sunflower-seed oil. In the lower register withdrawal of sunflower-seed oil was followed by a large rise in serum-cholesterol level. In the upper register both arachis oil and the unsaturated fraction prepared from sunflower-seed oil produced a similar response to that of sunflower-seed oil.

oil (iodine value 230), used industrially in the hardening of hardboard, appeared to be more effective than sunflower-seed oil in countering the effect of ten eggs daily (fig. 6).

USE OF SATURATED AND UNSATURATED FATTY-ACID FRACTIONS

In Supplementation of Hydrogenated Fat

These attempts might have been more convincing had we known earlier that the unsaturated fatty-acid fraction used in this experiment contained only 60–65% of linoleate. When this became known, the 100 g. of hydrogenated fat had to be supplemented with as much as 84 g. of this unsaturated fraction to achieve the desired 27% of linoleate, the estimated proportion in the non-hydrogenated oil. At this dosage there was insufficient for more than three days' feeding; but despite this great increase in the intake of fat, the serum-cholesterol level fell. On withdrawal of this unsaturated fraction the serum-cholesterol level rose again.

In Substitution for Sunflower-seed Oil

Apart from the experiment outlined above, the unsaturated fatty-acid fraction was fed to 1 European volunteer with coronary heart-disease in an attempt to reproduce the effects of the 100 g. of sunflower-seed oil and ground-nut oil supplements (fig. 4). In this volunteer the serum-cholesterol level promptly fell when these oil supplements were given, despite the continued consumption of the basic diet containing 50 g. of animal fat. When 50 g. of the unsaturated fatty-acid fraction (estimated linoleate content 37 g.) was added to this basic diet, no immediate effect was noted until a freshly prepared fraction was used. This delay, which may be attributable to isomerisation, is discussed below.

Rôle of Intake of Cholesterol with Highly Unsaturated and Saturated Fatty Acids

The effect of 100 g. of fat consumed as ten eggs far exceeds that of equivalent amounts of hydrogenated ground-nut fat (fig. 2). Eggs contain protein, cholesterol, and fat. In 1 volunteer (fig. 7) keeping the diet isonitrogenous by feeding casein after the withdrawal of the ten eggs did not maintain the rise in the serum-cholesterol level. The addition of 3 g. of cholesterol (equivalent to that in ten eggs) raised the serum-cholesterol level but not so high as it had been. When the quantitatively equivalent fat-content of ten eggs was supplied in a qualitatively dissimilar form (as sunflower-seed oil) the serum-cholesterol level fell despite the continued consumption of cholesterol and casein. On withdrawal of the sunflower-seed oil the serum-cholesterol level rose again. At this point 60 g. of the ethyl-linoleate fraction (the amount estimated to be present in 100 g. of sunflower-seed oil) given daily for six days reproduced these effects. When 15 g. of the saturated fatty-acid fraction from sunflower-seed oil was fed, the serum-cholesterol level rose sharply. At this stage the total intake of fat represented only 8% of the total calories.

The use of 30 g. of the saturated fraction in another subject was not associated with the same sharp rise. Over 18 days there was a gradual rise in the serum-cholesterol level from 100 to 145 mg. per 100 ml. From the eighth day of this period a more freshly prepared saturated fraction was given together with 0·6 g. of cholesterol, and the effect appeared to be more pronounced. The subsequent administration of massive doses (1000 mg. daily) of commercially prepared vitamin E ('Natopherol,' Abbott) in addition on the twenty-third day was not associated with an immediate fall in the serum-cholesterol level such as was seen with the pilchard oil; but six days later a slight fall occurred. (Not only was this dose far in excess of that present in natural oils but also the vehicle is an oil which may have a high unsaturated fatty-acid content.)

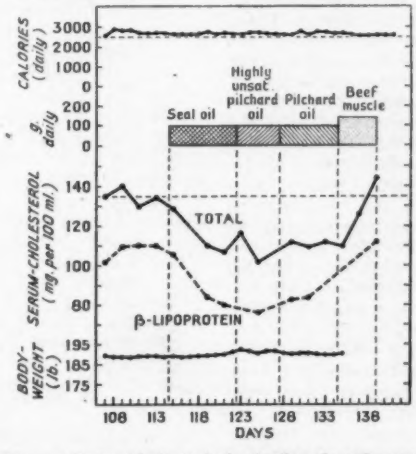

Fig. 5—In same Bantu as in fig. 3, during feeding of supplement of 100 g. of various marine oils the serum-cholesterol levels remained considerably lower than during the low-fat cholesterol-free control period. Substitution of beef muscle for marine oils was followed by a prompt rise in serum-cholesterol level.

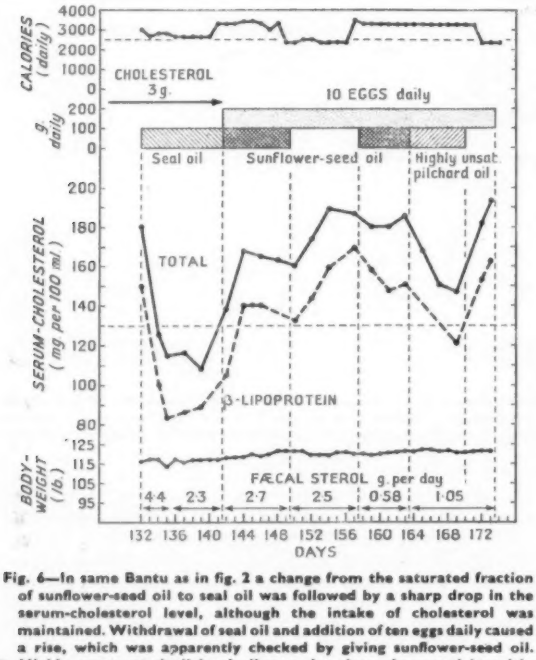

Fig. 6—In same Bantu as in fig. 2 a change from the saturated fraction of sunflower-seed oil to seal oil was followed by a sharp drop in the serum-cholesterol level, although the intake of cholesterol was maintained. Withdrawal of seal oil and addition of ten eggs daily caused a rise, which was apparently checked by giving sunflower-seed oil. Highly unsaturated pilchard oil caused a sharp drop, and its withdrawal was followed by a sharp rise.

We are currently investigating whether the saturated fatty-acid fraction alone, on the basic cholesterol-free diet, can raise the serum-cholesterol level.

OTHER DIETARY FACTORS

Vitamins

The 2 patients with scurvy had the lowest serum-cholesterol levels on admission. One of them was treated with vitamin C during the first olive-oil supplement, and no sudden change in the serum-cholesterol level followed. Later it was noticed that the cholesterol contained in the α-lipoprotein fraction may have increased, because the serum-cholesterol level did not return to its value before vitamin-C therapy. In the other patient with scurvy the lipoproteins were not fractionated on admission when he received vitamin-C therapy, but his serum-cholesterol level rose slowly and steadily during this period.

In the 2 cases with vitamin-B deficiency (one with beriberi and the other with pellagra) the serum-cholesterol levels fluctuated under treatment with vitamin-B complex on admission. Vitamin-B complex administered later and to the other volunteers did not affect the serum-cholesterol levels before periods of fat feeding.

Protein Intake

The changes that coincided with alterations in the intake of fat took place on protein-poor and on protein-rich diets. Increasing or decreasing the intake of protein by adjusting the intake of casein during the control period did not affect the serum-cholesterol levels. In some cases changes of this nature made a difference of more than 100 g. of protein. Furthermore by adjusting the intake of casein the diets in most instances could be kept isonitrogenous during feeding with supplements of different fats.

Calories and Changes in Body-weight

From the figures it will be seen that only minor changes in body-weight took place in most cases. A rapid gain in weight in 1 volunteer during the control period was not associated with changes in the serum-cholesterol level.

When the calorie intake was suddenly increased with an extra olive-oil supplement in 2 non-Europeans (fig. 1), and with sunflower-seed oil and marine fish and mammal oils in 2 other persons (figs. 3 and 6), the serum-cholesterol levels did not rise.

Discussion

In these short-term experiments changes in the serum-cholesterol levels coincided with changes in the intake of fat. The consistency of the results to date has not been affected by alterations in the protein, calorie, or vitamin intake. Brief reference to some of these findings has already been made (Bronte-Stewart et al. 1955b, 1956). The changes appeared to be more closely related to the quality rather than the quantity of the change in intake of fat.

In quantitatively equivalent amounts animal fats in the form of butter, beef dripping, beef muscle, and eggs caused a rise in serum-cholesterol levels. Marine animal oils had the reverse effect on the serum-cholesterol levels either when fed alone after a fat-free diet or with eggs.

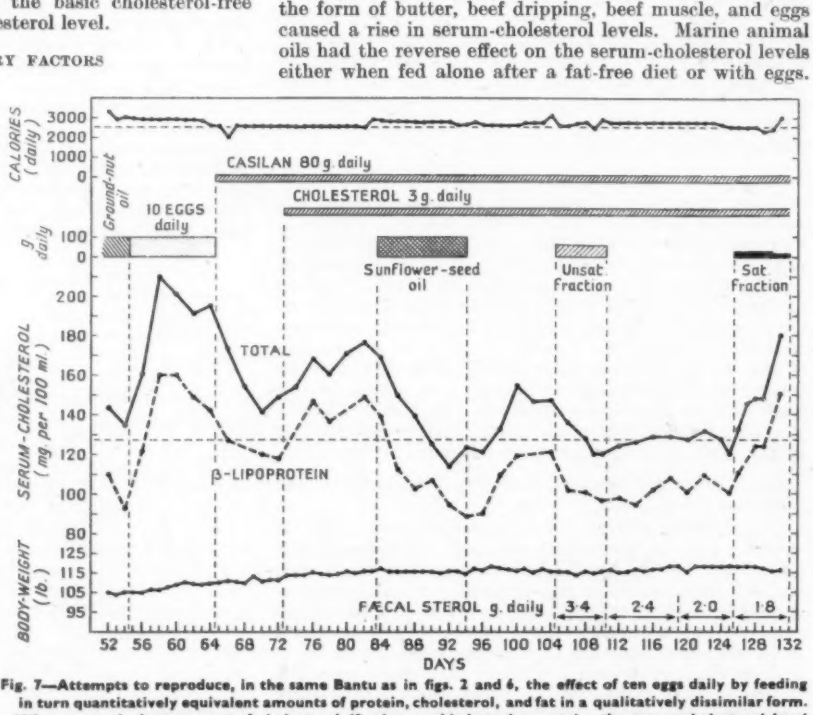

Fig. 7—Attempts to reproduce, in the same Bantu as in figs. 2 and 6, the effect of ten eggs daily by feeding in turn quantitatively equivalent amounts of protein, cholesterol, and fat in a qualitatively dissimilar form. When an equivalent amount of cholesterol (3 g.) was added to the protein, the serum-cholesterol level rose. Supplementation firstly with sunflower-seed oil (100 g.) and secondly with the unsaturated fraction from the same oil (60 g. of ethyl linoleate) produced a sharp fall in the serum-cholesterol level, which rose only when 15 g. of the saturated fraction was added (at this stage the total intake of fat constituted only 8% of the total calories).

Olive oil and ground-nut oil did not raise the serum-cholesterol levels. Ground-nut oil fed as the hardened or hydrogenated form behaved differently from the natural oil. This was regarded as a significant finding because one of the changes consequent on hydrogenation of oils is the destruction of the highly unsaturated fatty acids in their conversion to more saturated fatty acids which raises the melting-point (Deuel et al. 1951). The highly unsaturated fatty acid affected predominantly in ground-nut oil is linoleic acid, which has been regarded by Burr (1942) as an essential fatty acid having metabolic functions other than the supply of calories. Oleic acid and the saturated fatty acids did not appear to have these functions.

Other essential fatty acids listed by Burr (1942) are linolenic, hexahydroxystearic, arachidonic, and docosahexaenoic acids; the last-named two being present in high concentration in marine oils (Bailey 1945, W. S. Rapson personal communication). In a given dosage the biological activity of these latter essential fatty acids exceeds that of linoleic acid (Deuel 1955). Marine oils approach vegetable oils in their consistency at room-temperature and fatty-acid composition. They do not contain sitosterol and have a very low content of vitamin E, but the cholesterol content does not greatly differ from that of beef (Lange 1950).

Rôle of Dietary Intake of Cholesterol

We concur with the views of Messinger et al. (1950), Keys (1952), and Mayer et al. (1954) that the changes in the serum-cholesterol level are due to some factor additional to the cholesterol content of the dietary fat. Messinger et al. (1950) noted greater effects when the cholesterol supplement was given with cream; we believe that this supports our view that an additional factor is the type of fatty acid in the fat concerned. Our view is based on the fact that a possible common difference between animal fats and hydrogenated vegetable fat, on the one hand, and natural vegetable oils and marine oils, on the other, is not the cholesterol, sitosterol, vitamin, or protein content but is in some way connected with the proportion of highly unsaturated and saturated fatty acids in the fat concerned.

In feeding experiments on rats Swell and others (1955) found greater rises of the serum-cholesterol level when cholesterol was given with saturated fatty acids compared with unsaturated fatty acids. They emphasise the importance of the nature of accompanying fatty-acid intake in the esterification and absorption of cholesterol.

Our results with sunflower-seed oil (iodine value 130–138) containing about 60% of linoleic acid (Bailey 1945) are not unlike those described by Kinsell and Michaels (1955). In their diabetic patient the extent of the fall in the serum-cholesterol level could be related to the unsaturated fatty-acid content of the vegetable oil used. The most active was soy oil (iodine value 134) containing about 55% of linoleic acid and 6% of linolenic acid (Bailey 1945). Ahrens et al. (1955) too found that corn oil, an oil rich in linoleic acid, was effective in this regard.

Effect of Fatty-acid Fractions

It appears to us that the data obtained in these experiments may reasonably be explained by the concept that the fatty-acid composition of the fat consumed determines the effect on the serum-cholesterol levels. Whether the effects produced depend on the fatty acids or on some accompanying factor is not yet explained. Experiments with the pure fatty-acid fractions are being made, and a highly unsaturated fraction, when used soon after preparation, produced effects similar to those of sunflower-seed oil; this fraction was free from sitosterol but contained a little vitamin E. Although vitamin E in 1 volunteer appeared to produce a moderate fall of the serum-cholesterol level, the dosage used was far in excess of that present in vegetable oils; moreover this preparation (derived from vegetable oils) may be rich in unsaturated fatty acids. Vitamin E is not present in high concentration in marine oils, which nevertheless consistently depressed the serum-cholesterol level.

The unsaturated fraction that did not affect the serum-cholesterol levels had been redistilled in vacuo (±1 mm. Hg) three times and, on subsequent testing, was found to contain about 20% of conjugated linoleic acids formed by isomerisation either during distillation or in the initial saponification of the sunflower-seed oil. Burr (1942) has shown that the isomer of linoleic acid, 9–11 linoleic acid, has no biological activity.

The estimated vitamin-E content of this fraction was about four times that of the fresh unsaturated fatty-acid fraction that was effective later.

Possible Applications to Coronary Heart-disease

The magnitude of the problem of coronary heart-disease has prompted us to publish these preliminary results. Owing to difficulties in obtaining a sufficiency of the pure fatty-acid fractions, or the pure fatty acids contained therein, our results are incomplete, but they show a very consistent trend.

This consistency has applied particularly to the depressant effect on the serum-cholesterol level of oils with high unsaturated fatty-acid content. On feeding supplements of animal fat the serum-cholesterol levels were consistently raised, but not so high in the post-hemiplegic patient as in the others. This raises the possibility that individuals may vary in their response to the dietary intake of fat.

The serum-cholesterol levels usually changed within forty-eight hours of the dietary change, which is the time taken for the specific activity to reach its peak in isotope studies (Hellman et al. 1955). Although the length of the feeding periods varied, it is quite possible that different effects might have been observed if these experiments had been continued longer.

The application of these findings to certain problems in the ætiology of coronary heart-disease depends on the acceptance of the views that coronary heart-disease is in part a disorder of cholesterol and related lipoid metabolism, that there is a relationship between natural atherosclerosis in man and experimental atherosclerosis in laboratory animals, and that epidemiologically there is a relationship to the dietary intake of fat.

Metabolism

The interrelationship of the essential fatty acids and cholesterol metabolism is becoming well documented (Kelsey and Longenecker 1941, Alfin-Slater et al. 1954, Deuel 1955, Peifer and Holman 1955, Shapiro and Freedman 1955, Swell et al. 1955). Apart from the different sex requirements in the younger age-groups (Cheng et al. 1952) there are reported differences in capillary permeability and fragility which can be reversed by changing the intake of fat from animal to vegetable in man and by feeding ethyl linoleate in the rat (Kramár and Levine 1953).

Kritchevsky et al. (1954) noted lower serum-cholesterol levels and less atherosclerosis in rabbits fed cholesterol with 9% corn oil (iodine value 130) compared with rabbits on comparable cholesterol diets with 9% hydrogenated fat (iodine value 92). The possibility exists that atherosclerosis is intensified by a dietary deficiency of essential fatty acids. In support of this theory is the finding of Alfin-Slater et al. (1954) of an increase in cholesterol ester in the livers of rats on low-fat diets. On the other hand, Hartroft (1955) has reported increased deposition of fat in the liver when the intake of saturated fatty acids is high. It is therefore of interest that, in man, Hammond and Lundberg (1955) have demonstrated differences between the fatty-acid content of the blood of atherosclerotic patients and blood-donors, the former having a lower proportion of linoleate and arachidonate.

Epidemiology

Inter-racial studies (Keys and Anderson 1954) and the drop in mortality during the German occupation of Norway (Malmros 1950, Strøm and Jensen 1951) have been largely responsible for the general acceptance of the dietary-fat theory of coronary heart-disease. This is always countered by reference to the fat-eating Eskimo (Page 1954, Schmidt 1955). Sinclair (1953) has shown that the diet of the Eskimo consists predominantly of seal, fish, and other marine animals—an intake of fat characterised by a high content of unsaturated fatty acids—but the Eskimo diet apparently varies from area to area (Scott 1956). Fish is a major factor in the diet of the Japanese, who have one of the lowest death-rates from coronary heart-disease in the world (Keys and Anderson 1954). Coronary heart-disease is not prevalent in the olive-oil-eating Latin peoples or in primitive communities such as Africa and China, where maize, soybean, and sunflower seed allow the amount of unsaturated fatty acid to exceed that of saturated fatty acid in the diet (Tuttle 1952).

In more civilised and prosperous areas developments in animal husbandry are aimed at the greater priming of beef, improvements in egg production by battery farming, &c., and greater yields of dairy produce. Moreover butter from stall-fed cows contains less iodine and linoleate than does that from cows feeding in summer pastures (Bailey 1945). More and more people are allowed the opportunity for over-indulgence in saturated fatty acids. The consumption of saturated fatty acids is increasing (Fullerton 1955), often at the expense of the unsaturated fatty acids owing to the processing of natural foodstuffs. Hydrogenation of vegetable oils is a recent luxury for the housewife and processed breakfast cereals are superseding porridges, with consequent loss of the natural oil contained in the germ.

The decrease in mortality during the German occupation of Norway was associated not only with decreased consumption of animal fat but also with bomb damage to hydrogenation plants.

The yearly increasing incidence of coronary heart-disease is seen in females as well as in males, and the death-rate in European females exceeds by far that in Bantu males (Phillips 1956). There must therefore be a factor additional to the circulating œstrogens of the female.

It is as well to re-emphasise that the present work has done no more than illustrate that the serum-cholesterol level may be influenced by the nature of the fatty acids in the diet. The results of these short-term feeding experiments agree with the findings of the inter-racial survey reported earlier (Bronte-Stewart et al. 1955a), which imply that the customary dietary habits of communities may be reflected in their mean serum-cholesterol levels. The evidence that the dietary fat influences the development of coronary heart-disease in man, although strong, is purely circumstantial and has been derived mainly from epidemiological studies. The nature of the fatty acids constituting the dietary fat may provide the basis for a better hypothesis. We agree that to attribute this disease to a single cause would be a cardinal error at this stage (*Lancet* 1955). If, however, the nature of the modern diet is a major factor in the development of coronary heart-disease, there is hope that this disease may eventually be controlled and prevented.

Summary

To confirm the findings of an inter-racial survey in this area (Bronte-Stewart et al. 1955a), we fed several different fats and oils to volunteers under controlled conditions and studied the effect on the serum-cholesterol levels.

Animal fats and hydrogenated vegetable fat behaved differently from vegetable and marine fish and mammal oils. The most likely common difference between these fats and oils is the proportion of unsaturated and saturated fatty acids in the fats and oils concerned.

Sunflower-seed oil and a segregated highly unsaturated fatty-acid fraction from pilchard oil have, in the persons studied, consistently depressed the serum-cholesterol levels when fed alone, with a supplement of cholesterol, or with one of animal fat.

The possible application of these findings is discussed, and it is suggested that certain discrepancies in the dietary-fat theory of the ætiology of coronary heart-disease may be explained by variations in the nature of the fatty-acid composition of the fats concerned.

This study was undertaken as part of the programme of the Research Unit in Clinical Nutrition supported in the University of Cape Town by the South African Council for Scientific and Industrial Research. We wish to thank Dr. Ancel Keys, of the University of Minnesota, for his suggestions at the outset of these studies, and Dr. W. Odendaal, of the National Nutritional Research Institute, Pretoria, for the advice given later. Technical and other assistance was given by Mrs. C. Damstra, B.SC., Miss J. Ethelston, B.SC., Miss C. Solms, Miss E. Volks, B.SC., Mrs. A. Betts, Mrs. E. Pallett, Dr. M. Fewster, Mr. T. J. Turner, Mr. R. Thompson, Mr. D. Brock, Mr. G. F. J. Schoonraad, and the staff of the Metabolism Unit. We wish to thank also the directors and chief chemists of Messrs. Lever Bros. (S.A.) (Pty.) Ltd., Marine Oil Refiners of Africa Ltd., and the Government Guano Island authorities for the supply of fats and oils and other valuable assistance given. Finally we should like to record our gratitude to our volunteers, who consumed on many occasions malodourous oils without demur.

ADDENDUM

Since submitting this paper we have seen Sinclair's (1956) stimulating analysis of the possible rôle of deficiency of essential fatty acids in the ætiology of atheroma, &c. We cannot comment critically on his analysis here, but we are intrigued by some of the possibilities which it raises in interpretation of our own experiments with fats of differing degrees of saturation.

We have also seen the detailed report of the Minnesota Arteriosclerosis Symposium. The pronounced fall in serum-cholesterol levels reported by Malmros and Wigand (1955) in eight cases of familial hypercholesterolæmia accompanied the institution of a diet rich in corn oil. They felt these effects might possibly be due to the high essential fatty acid content of corn oil (57% linoleic acid).

These views are in line with our short-term investigations of the effects of hydrogenated and natural fats and oils which we suggest are related to their unsaturated/saturated fatty-acid content.

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TREATMENT OF TETANUS

SEVERE BONE-MARROW DEPRESSION AFTER PROLONGED NITROUS-OXIDE ANÆSTHESIA

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SINCE the 1952 epidemic of poliomyelitis in Copenhagen the therapeutic measures introduced in the management of the life-threatening forms of infantile paralysis have been adapted to several other diseases presenting similar problems—e.g., tetanus.

Bjørneboe et al. (1953) were the first to describe a severe case of tetanus cured by treatment along these lines, and Lassen et al. (1954) gave a detailed account of 4 such cases. Since then cases have been published by Shackleton (1954), Forrester (1954), Haglund (1955), and Mollaret et al. (1955).

When the conventional treatment of tetanus with barbiturates, chloral hydrate, or bromethol does not totally suppress the spasms, or if adequate ventilation is threatened by accumulation of secretion in the upper respiratory passages, eventually followed by atelectasis, a high tracheotomy under general anæsthesia preceded by oral intubation should be done and an inflatable rubber cuff-tube inserted into the trachea.

This procedure secures against suffocation due to laryngeal spasms or tetanic standstill of the respiratory muscles. At the same time aspiration through the tube makes it possible to keep the airway free from secretions.

Convulsions and rigidity can be kept in check with *d*-tubocurarine chloride given either continuously through an intravenous drip or by repeated intravenous injections. When, however, convulsions are severe, the requisite dosage of tubocurarine invariably produces inadequate ventilation because of failure of the respiratory muscles, and artificial respiration (some kind of positive-pressure ventilation) becomes necessary.

Tetanus does not affect the patient's mental state, nor does curare. In severe curarised cases, therefore, the patient is totally paralysed but fully conscious, aware of everything that is going on around him, and no doubt subjected to great emotional strain. He appears stuporous, cannot talk, and, since even the slightest movement of the muscles is suppressed, cannot communicate with anybody by either gestures or facial expression. The treatment of tetanus often has to be continued for many weeks, and we tried to find ways to avoid the long-continued psychological strain. For this purpose nitrous-oxide anæsthesia seemed ideal. It produces a mild narcosis, which reduces the need for curare and sedatives. No harmful side-effects are known, and the anæsthetic is easy to administer continuously to patients on spontaneous respiration as well as to patients on artificial respiration. In most cases we used a mixture of 50% oxygen and 50% nitrous oxide.

Hæmatological Complications

The first 2 patients treated on these lines were cured and left the hospital without sequels. Severe tetanus is thus a self-limited disease, and all its symptoms and all complications are reversible.

At that time we felt rather optimistic, but further experience proved us to be too optimistic. The 3rd patient treated in this way was a boy aged 15 with fulminant tetanus. After seventeen to eighteen days' treatment the tetanus subsided, continuous anæsthesia with nitrous oxide and oxygen was discontinued, medication with curare was stopped, and he only needed moderate doses of chloral hydrate to keep him relaxed. But at this time signs of aplastic anæmia developed.

Fig. 1 shows that, despite repeated blood-transfusions, pronounced granulocytopenia and thrombocytopenia with

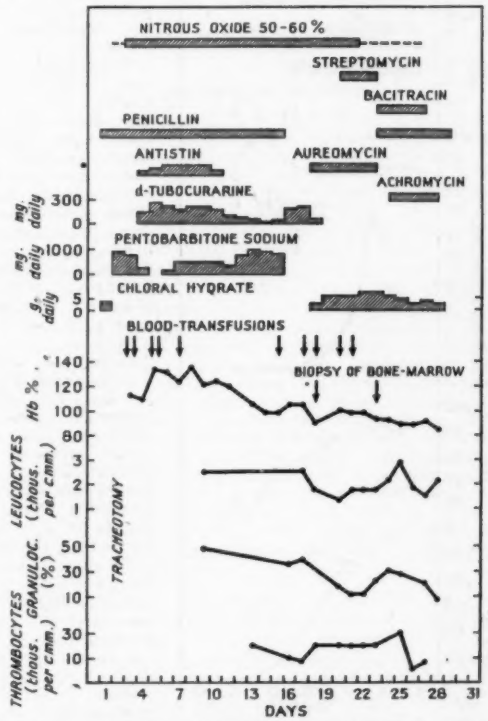

Fig. 1—Changes in peripheral blood in relation to medication in a boy, aged 15, with severe tetanus.

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severe hæmorrhagic diathesis developed followed by septicæmia due to *Escherichia coli* and *Pseudomonas pyocyanea*. Electrocardiography showed pronounced myocarditis. Bone-marrow biopsy revealed severe damage to the blood-forming cells "presumably due to some drug or other." A few days after the anæsthesia had been discontinued signs of remission developed in the bone-marrow, yet on the twenty-ninth day the boy died from cardiac insufficiency and septicæmia.

When we reviewed the case-histories of the first 2 patients, who had recovered, it became clear that they also had shown signs of hæmatological complications. The 1st, a boy aged 10 years, had thrombocytopenia, hæmaturia, and retinal hæmorrhage on the fourteenth day of treatment. In the 2nd case, that of a boy aged 11 years, between the sixth and tenth days in hospital the leucocyte-count fell from 12,500 to 2200 per c.mm. Treatment was discontinued on the twelfth day, and the blood was not examined again.

The 4th patient had moderately severe tetanus, and hæmatological complications did not appear.

In March, 1955, a 5th patient, a woman aged 53, was admitted with severe tetanus.

Very early after admission tracheotomy had to be done. After the operation she was treated according to the principles previously outlined, including anæsthesia with nitrous oxide and oxygen.

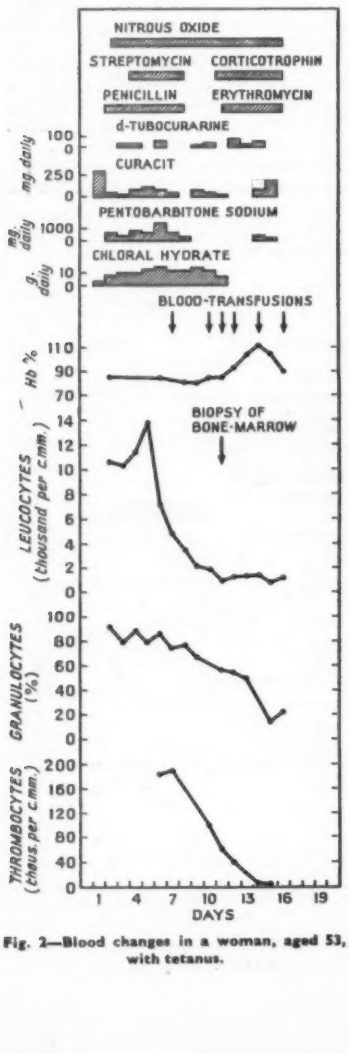

Fig. 2—Blood changes in a woman, aged 53, with tetanus.

Fig. 2 shows how the tetanus gradually subsided and the dosage of sedatives was reduced considerably. Blood-counts were made daily, and already on the fifth day a pronounced granulopenia was observed, and this was soon followed by thrombocytopenia.

Pentobarbitone was suspected of having depressed the bone-marrow. On the eleventh day, therefore, it was withheld. This did not have any effect. On the same day a bone-marrow biopsy showed: "Hypoplastic bone-marrow with reduced erythropoiesis of megaloblastic type; granulopoiesis with a pronounced shift to the left; and numerous myeloid cells of undetermined character." The pathologist concluded that all the observed changes might be due to severe drug allergy.

Treatment with large doses of vitamin B_{12} was instituted on the thirteenth day, but no increase of reticulocytes or other sign of remission was observed. In all other respects the treatment remained unchanged. Septicæmia caused by *Esch. coli* now developed, and the patient died on the sixteenth day with signs of severe hæmorrhagic diathesis. Post-mortem specimens of bone-marrow revealed "pronounced atrophy with greatly reduced or probably totally abolished myelopoiesis."

CHANGES IN PERIPHERAL BLOOD IN RELATION TO DRUGS USED IN PATIENTS WITH SEVERE TETANUS

Treatment	Granulocytopenia and/or thrombocytopenia	No hæmatological complications
Chloral hydrate	3	7
Pentobarbitone sodium	5	5
'Phenemal' sodium	0	1
Pethidine	0	1
d-Tubocurarine	3	0
Bromethol	0	1
'Curacit'	1	0
'Largactil'	1	0
Continuous nitrous oxide	6	0

Gormsen (1955) published a case of severe tetanus showing agranulocytosis and thrombocytopenia in a boy treated by prolonged anæsthesia with nitrous oxide and oxygen, chlorpromazine, and curare. In this case also a reduced number of leucocytes in the peripheral blood was observed on the fifth day of treatment, followed by a decrease in the number of thrombocytes. Gormsen presumed that the hæmatological changes were due to the large doses of curare.

It thus became clear that the complex treatment to which our patients with tetanus had been submitted produced with great regularity signs of acute depression of the bone-marrow at the end of the first week of treatment. What could the cause be? Did extremely severe tetanus cause bone-marrow damage which had hitherto been unobserved because formerly these patients died? Or was it due to the heavy dosage of pentobarbitone? Or chloral hydrate used for several weeks? Could nitrous-oxide anæsthesia continued for many days be responsible despite the accepted innocuousness of this widely used anæsthetic agent? Or could the hæmatological complications be traced back to the large doses of curare used over several weeks?

In an attempt to detect the cause we have studied 13 cases of tetanus, most of them of short incubation and rapid evolution.

In the accompanying table the cases have been divided into two groups: with and without granulocytopenia and thrombocytopenia. In the first group all the patients underwent tracheotomy, but in the second group only 6 of 8. This fact shows that the cases in group 1 were more severe than those in group 2. The difference, however, is not pronounced; hence the conclusion that the hæmatological complications could be due to the severity of the tetanus seems unlikely. Nor were signs of a hyperimmunising effect observed with abnormal hæmolysis, and electrophoresis did not reveal an increase of the gamma-globulin fraction of the serum-proteins.

The possibility remained that one or other of the drugs used was responsible.

The table shows that only nitrous oxide was a common factor in the treatment of all the patients who presented blood changes. The use of the other drugs—e.g., pentobarbitone—was equally distributed in both groups, or else they were used only sporadically. Suspicion was thus directed towards the anæsthesia, and the fact that the hæmatological complications regularly appeared from five to seven days after its introduction further incriminated the nitrous oxide.

The extensive literature on nitrous oxide contains no information about toxic effects on the bone-marrow. This anæsthetic, in fact, is considered completely

innocuous. After considerable discussion in the correspondence columns of this journal Sykes (1955) declared: "I am aware of no work which suggests that nitrous oxide per se is dangerous." This statement, of course, applies only to the usual surgical use of nitrous oxide and not to its use over many days.

In view of the fact that our first 2 patients who recovered had shown signs of bone-marrow depression, and thus had proved that the hæmatological changes were not invariably fatal, it was felt permissible to try the effect of prolonged anæsthesia with nitrous oxide and oxygen under strict hæmatological control.

Clinical Trial of Nitrous-oxide Anæsthesia

On Sept. 1, 1955, a boy, aged 10 years, was admitted with severe tetanus.

Twelve days previously he had been run over by a tractor and had sustained a compound fracture of his right leg. Trismus and severe backache appeared ten days later, but despite this rather long incubation time severe tetanus developed with alarming rapidity.

On the day after admission respiration became inadequate through accumulation of secretion in the airway and incipient atelectasis, and tracheotomy had to be done. During the next two weeks the tetanus was kept in check with pentobarbitone given through an indwelling stomach-tube. Because of the severity of the tetanus the dosage of the pentobarbitone had to be so large that spontaneous respiration failed and it became necessary to institute manual artificial respiration or to use a positive-pressure machine.

Fig. 3 shows that during the first two weeks' treatment the leucocyte and thrombocyte counts and granulocyte percentage remained normal. General anæsthesia was then started with 50% nitrous oxide and 50% oxygen and immediately proved beneficial. The tetanus promptly became more easy to handle, and the dosage of sedatives was reduced.

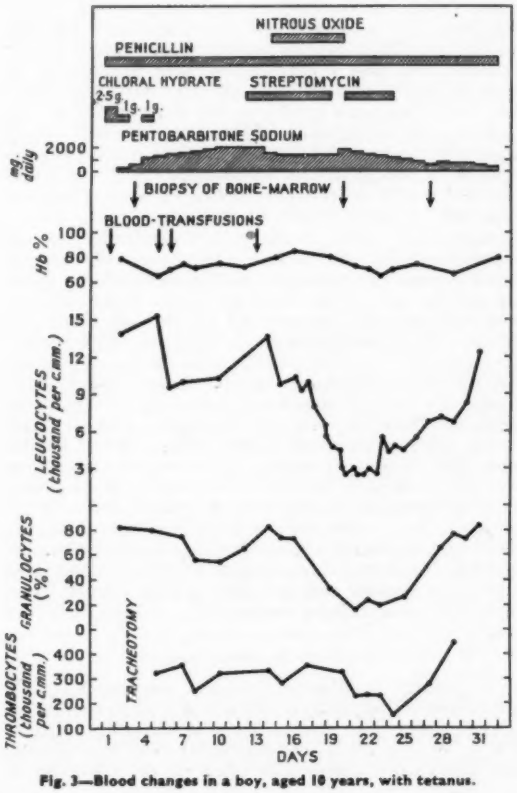

Fig. 3—Blood changes in a boy, aged 10 years, with tetanus.

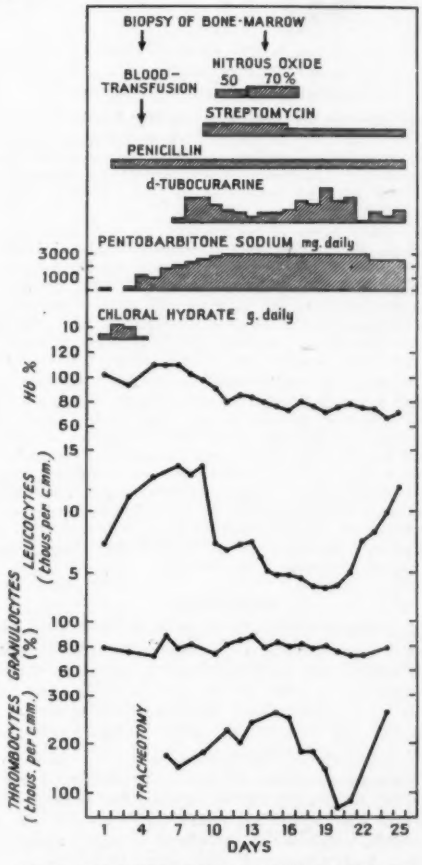

Fig. 4—Blood changes in a girl, aged 13, with tetanus.

On the fourth day of nitrous-oxide anæsthesia the percentage of granulocytes decreased so sharply that next day the administration of nitrous oxide was discontinued. In the next few days a rather considerable decrease in the number of thrombocytes was also observed.

Bone-marrow biopsy on the fifth day of anæsthesia revealed that erythropoiesis was strikingly megaloblastic and the changes in granulocytopoiesis were so pronounced and typical that, unless one knew the clinical history, one would not hesitate to diagnose pernicious anæmia.

After the anæsthetic had been discontinued we followed the course of the tetanus with apprehension although the boy's general condition was satisfactory. On the next three days the leucocyte-counts remained low. The tetanus became active and the doses of sedatives had to be increased. On the fourth day, however, the number of leucocytes began to increase although transfusion and anti-pernicious-anæmia drugs had not been given and the general régime remained unchanged. A few days later the white-cell count was normal, and bone-marrow biopsy showed changes consistent with toxic-infectious damage, and no signs of lack of anti-pernicious-anæmia factor. The further course of the tetanus was uneventful, and the boy was transferred to the local hospital a few weeks later.

At this juncture Mollaret et al. (1955) published a severe case of tetanus in which agranulocytosis developed after the patient had been treated by tracheotomy and artificial respiration and with chlorpromazine, *d*-tubocurarine, and various sedatives, but no nitrous-oxide anæsthesia. Only the white cells (especially the granulocytes) were involved; apart from this the bone-marrow was normal (R. Bastin, personal communication).

This fact made it desirable to repeat the experiment just described.

On Nov. 5, 1955, a girl aged 13 was admitted with rapidly progressing tetanus seven days after she had scratched the ankle on a soiled wooden board.

After admission her condition rapidly became worse, and on the third day tracheotomy had to be done because of repeated episodes of cyanosis. Sternal biopsy under general anæsthesia showed non-specific toxic-infectious changes in the bone-marrow without signs due to lack of anti-pernicious-anæmia factor (fig. 4).

Despite huge doses of pentobarbitone and *d*-tubocurarine it was difficult to prevent convulsions and impossible to attain permanent relaxation. On the ninth day general anæsthesia with 50% nitrous oxide and 50% oxygen was begun. Nevertheless the patient still had occasional convulsions and long spells of pronounced rigidity, which made us increase the nitrous oxide to 70% of the gas mixture, and for the first time we were able to keep her completely relaxed.

On admission the white-cell count was 7000 per c.mm. A few days later the count rose to 14,000 per c.mm., probably owing to infection in the airway and atelectasis. When nitrous-oxide anæsthesia was instituted, the number of leucocytes was normal and rather constant. Four days later the count fell to 2700 per c.mm. and the thrombocyte-count fell to 70,000 per c.mm. Bone-marrow biopsy again showed the changes now considered to be typical: depression of erythropoiesis of megaloblastic type. Nitrous-oxide anæsthesia was now discontinued, and three days later incipient hæmatological remission was observed.

Comments

We have felt it our duty to publish these preliminary observations as quickly as possible because it was we who advocated the prolonged use of nitrous oxide in severe tetanus (Lassen et al. 1954). We now draw attention to the fact that, when nitrous oxide is used continuously for five or six days, acute bone-marrow aplasia is likely to develop.

The changes observed in our cases followed the use of commercial nitrous oxide, which (according to the analysis of the manufacturers) contains 99·7% pure nitrous oxide, insignificant amounts of argon and carbon monoxide, and traces of unknown impurities. This commercial product is used for ordinary nitrous-oxide anæsthesia all over Denmark without ever having been known to cause harmful side-effects.

Experiments on animals have now been started, and we hope shortly to be able to throw further light on this problem. Hitherto it has been impossible to obtain nitrous oxide 100% pure.

Summary

Patients with severe tetanus were treated by tracheotomy and prolonged nitrous-oxide anæsthesia and with sedatives and curare.

In the course of treatment various hæmatological complications were observed, and fatal aplastic anæmia developed in 2 patients.

These observations and two trials on patients with tetanus led us to conclude that prolonged anæsthesia with nitrous oxide may cause acute aplasia of the bone-marrow. The bone-marrow changes rapidly disappear when this anæsthetic agent is discontinued.

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ADRENALECTOMY FOR VASCULAR DISEASE OF DIABETES

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ADRENALECTOMY in a diabetic was first reported by Green et al. (1950). The patient had malignant hypertension which responded favourably although the adrenalectomy was incomplete, and fair health was maintained with low-dosage substitution treatment. Wortham and Headstream (1953) gave a short follow-up account of 7 further patients with advanced diabetic vascular disease, which they reviewed a year later (Wortham and Headstream 1954). The results were mildly encouraging in view of the refractory nature of the lesions for which the adrenalectomy had been done.

Adrenalectomy for diabetic vascular disease rests, perhaps, on somewhat slender theoretical supports. The case reported by Poulsen (1953) of recovery from retinopathy in a patient with diabetes and Simmonds's disease drew attention to the possibilities of modifying vascular disease by reducing pituitary or adrenal function but has been made to bear too great a significance for an isolated observation:

A woman, diabetic from the age of 9 years, had retinopathy at the age of 30; she was then pregnant, and after delivery typical Simmonds's disease developed. Her insulin sensitivity greatly increased, and her tendency to ketosis ceased. At the age of 34 her retinopathy was less, and at the age of 36 it was no longer visible. Now, when she is aged 40, Poulsen (1955) reports that this improvement is maintained.

Lukens and Dohan (1946) produced typical lesions of diabetic glomerulosclerosis by maintaining experimentally produced pituitary-diabetes in a dog for five years, and Becker (1952) claims to have produced retinal micro-aneurysms by injecting corticotrophin into alloxan-diabetic rabbits. Marble (1954) could not confirm Becker's work, and in the clinical field Ricketts et al. (1949) examined patients considered to have "steroid" diabetes of Cushing's syndrome but did not find a high incidence of retinopathy. However, Becker (1952) suggested that repeated adrenal cortical overactivity in response to swing of the blood-sugar level (in either direction) might be the mechanism by which vascular complications are produced in diabetes.

Kinsell et al. (1954), working on a similar hypothesis, prefer hypophysectomy in young diabetics with vascular disease because this operation renders the diabetes stable and easy to control and therefore might be expected to arrest the vascular damage by cutting off stimuli to adrenal cortical overactivity. In 5 patients with reasonable kidney function the control of the diabetes was made more easy and progress of vascular disease seemed to be arrested six months after hypophysectomy. Luft et al. (1955) said that they did hypophysectomy to eliminate "those anterior pituitary factors which animal experiments have shown to possess a diabetogenic action, as these hormones might be connected with the development and/or progression of the vascular disorders." Of 19 patients 7 died within twenty months of operation. In a follow-up of survivors from three to forty-three months the renal disease and the retinopathy were not considered to have progressed, and in a few of them it may have improved. The blood-pressure was reduced in every case.

Present Investigation

The gravity of diabetic vascular disease in young patients seemed to justify a trial of one of these operations. Adrenalectomy was chosen for the following reasons: (1) it is, on the whole, less damaging than hypophysectomy and carries a negligible risk; (2) the maintenance

TABLE I—CLINICAL DATA

Case no.	Sex	Age (yr.)	Estimated duration of diabetes (yr.)	Duration of vascular disease (retinopathy) (yr.)	Albuminuria (g. per litre)	"Severity" of diabetes (units of insulin)	Control (5 yr.)
1	M	31	20	5	5	24	"Brittle"
2	M	49	30	13	..	40	Good
3	M	53	23	6?	4	30	Good
4	M	60	?	?	1	36	Good (1 year only)
5	F	57	20	2	..	16	Fair
6	F	53	?	?	..	52	Good (2 years only)

programme is simpler; (3) the preoperative and postoperative management of adrenalectomy was already well understood at the hospital to which the diabetic clinic was attached; and (4) intractable hypoglycæmia after hypophysectomy had been reported (E. B. C. Hughes, W. G. Oakley, personal communications).

Material

6 patients were subjected to total adrenalectomy for diabetic vascular disease at the General Hospital, Birmingham. The main facts are set out in tables I and II.

In case 1 there had for years been fluctuation between abnormally high and low blood-sugar levels, though ketosis requiring admission to hospital had only occurred once. Cases 2 and 3 had no glycosuria in fasting specimens, and the blood-sugar level at 2 P.M. was below 180 mg. per 100 ml. at each attendance. The duration of the retinopathy in case 3 was unknown because he only began to attend hospital six years before admission, when

TABLE II—FINDINGS BEFORE OPERATION

Case no.	Stage of retinopathy (Ballantyne)	Albuminuria (g. per litre)	Blood-urea (mg. per 100 ml.)	Blood-pressure (mm. Hg)	Indication for operation
1	3	8	220	180/110	Retinopathy: failing vision
2	3	0	39	150/80	Retinopathy: vitreous hæmorrhages
3	4	5	50	200/100	Retinopathy: vitreous hæmorrhages; albuminuria
4	4	2	41	200/100	Retinopathy: failing vision; albuminuria
5	3	0	38	210/130	Retinopathy: vitreous hæmorrhages
6	3	0	28	140/80	Retinopathy: failing vision

he already had retinopathy. Case 4 was only found to have diabetes two years before admission, when the retinal changes impaired his vision. Case 5 had been well controlled by dietetic restriction for the first fourteen years of her diabetes, but for the last six years only symptomatic control had been maintained: there was glycosuria in all specimens of her urine, and her average blood-sugar level at 2 P.M. was 250 mg. per 100 ml. Case 6 had been treated for two years following the discovery of advanced retinopathy, though glycosuria had been first found twenty-eight years earlier.

Retinopathy is graded by Ballantyne's classification: (1) micro-aneurysms singly or in small numbers near the macula; (2) blot hæmorrhages and confluent waxy exudates; (3) addition of venous changes: tortuosity, loops, coils, and plexuses on the anterior surface of the retina or in the vitreous; and (4) intraocular hæmorrhage preventing ophthalmoscopy, blindness, and perhaps glaucoma. In cases 1, 3, and 4 there was no reason to doubt that the hypertension was renal in origin. In case 5 a gradual rise of blood-pressure had been noted throughout ten years; there was a family history of high blood-pressure, and the hypertension was regarded as "essential."

Operations

All the operations were done by Mr. J. A. C. Edwards in two stages by the lumbar approach, and in every case the adrenal glands were believed to have been removed entire. The preoperative and postoperative routines were the same in every case, and were applied to both the first and the second stages:

(1) Soluble insulin in divided doses was used for three days before the operation to avoid any depot effect of long-acting

TABLE III—RESULTS OF OPERATION

Case no.	Follow-up	General state	Diabetic control	Retinopathy	Albuminuria	Insulin (units)	
						Before	After
1	2 weeks (died)	..	..	..	..	24	..
2	16 months	Better	Unchanged	Better	..	40	44
3	9 months	Unchanged	Unchanged	Unchanged	Unchanged	36	20
4	11 months	Unchanged	Unchanged	Unchanged	Unchanged	36	44
5	9 months	Unchanged	Better	Worse	..	16	16
6	5 months	Unchanged	Unchanged	Unchanged	..	52	48

preparations. On the morning of the operation soluble insulin in a dose of a third of the normal daily total was given with glucose 30 g. three hours before the operation. On the day following the operation a dose of a quarter of the normal daily total was given, and on the second postoperative day treatment with delay insulin was resumed.

(2) Twelve hours before the operation intramuscular cortisone 200 mg. was given, and 50 mg. by the same route six-hourly for the following forty-eight hours. Cortisone 25 mg. was given orally three hours before the operation, then no more until the second postoperative day, when four doses of 25 mg. were given, the dosage thereafter being gradually decreased to 50 mg. daily.

(3) During the operation and the following twenty-four hours an intravenous infusion of 4 pints of physiological saline solution was given. Glucose was not used, because it makes estimations of the blood-sugar useless. By the second day a full diet was resumed, and thereafter no special modification of the diet was used.

Results

The major effects of the operations are set out in tables III and IV. "General state" refers to the sense of well-being, maintenance of body-weight, and capacity to work. The improvement in case 2 partakes of all these features, with a return to normal visual acuity.

TABLE IV—FINDINGS AFTER OPERATION

Case no.	Stage of retinopathy		Albuminuria (g. per litre)		Blood-urea (mg. per 100 ml.)		Blood-pressure (mm. Hg)	
	Before	After	Before	After	Before	After	Before	After
1	3	3	8	..	220	..	180/110	..
2	3	3	0	0·0	39	35	150/80	120/80
3	4	4	5	5·0	50	40	200/100	150/80
4	4	4	2	1·8	41	45	200/100	180/80
5	3	4	0	0·0	38	28	210/130	150/80
6	3	3	0	0·0	28	30	140/80	130/80

The unchanged state of cases 3–6 may not be an entirely negative result. Certainly in cases 3 and 4 a further deterioration as a result of renal disease was to be expected, even within the limited follow-up.

Control of Diabetes

It is difficult to calculate, except in general terms, any change in the ease with which the diabetes was controlled. These patients after operation were attending frequently and were under close observation; hence adjustments of insulin dosage or of diet were readily made. There did not appear to be any significant difference in average blood-sugar level, total glycosuria daily, or incidence of hypoglycæmia after the operation, except in case 5, who achieved an average blood-sugar level of 150 mg. per 100 ml. and a daily output of less than 5 g. of glucose on the same dosage of insulin—16 units daily. Possibly the improvement was entirely due to improved care with diet. The patient has had one attack of insulin coma, due to delay of a meal, since operation. This is the only major episode of hypoglycæmia in the whole series.

Insulin Dosage

In Wortham and Headstream's (1953, 1954) series the insulin dosage after adrenalectomy was two-thirds of that before operation. After hypophysectomy in Olivecrona's series (Luft et al. 1955) the average was from a quarter to a third of the preoperative dosage. In the present series there was no significant reduction in insulin dosage. This may be due to the use of a comparatively large maintenance dosage of cortisone (50 mg.). The possibility of supplementing a lower dosage with deoxycortone acetate was considered but rejected. Luft et al. (1955) no longer use deoxycortone acetate, because of its unfavourable effect on damaged blood-vessels.

Retinopathy

In case 2 vitreous hæmorrhages, which were taking place at least once a fortnight, have ceased, there being no recurrence since the operation. The appearance of retinitis proliferans persists, but the visual acuity in each eye is 6/6. In cases 3 and 4 there has been no detectable change in the retinopathy; but, since massive vitreous hæmorrhage had already obscured the fundus, it is impossible to be certain.

In case 5 fresh vitreous hæmorrhage recurred two months after the operation and was followed by glaucoma with total loss of vision in the left eye. Fortunately the right eye, amblyopic because of a squint, was only slightly affected by retinopathy, and the visual acuity is slowly improving. Case 6 has been followed for only four months, and the absence of change is not significant.

Albuminuria

Apart from case 1, already in advanced renal failure, cases 3 and 4 have shown no sustained improvement in daily albuminuria. Six months after the operation both showed a significant decrease—from 5 to 2 g. and from 2 to 0 g.—but three months later there had been a return to the preoperative levels.

Blood-pressure

In cases 3 and 4 there was no reason to doubt that the hypertension was renal in origin; the reduction in blood-pressure cannot be considered significant after so short a follow-up. In case 5 a rising blood-pressure had been noted for seven years, and a diagnosis of essential hypertension was accepted.

Discussion

If these results are considered in conjunction with those of Wortham and Headstream (1953, 1954), certain conclusions may be advanced in spite of the small number of patients; they are those which common sense suggests:

(1) The operative mortality of total adrenalectomy in patients with diabetic vascular disease not having renal failure is negligible.

(2) Maintenance with cortisone after total adrenalectomy is simple.

(3) The general health is not made worse by total adrenalectomy.

(4) Control of the diabetes is unaffected by total adrenalectomy.

(5) Retinopathy and renal damage may be halted at an early stage; this cannot be established until after a longer follow-up. Advanced retinopathy is not altered, and renal failure, if established, is accelerated.

Selection of Material

It is now generally agreed that the most urgent clinical problem in diabetes is the vascular disease which seems to develop inevitably if the patient lives sufficiently long. Those whose diabetes starts after the age of 50 may live to old age without apparent acceleration of arterial degeneration, but the young are condemned to certain death from a characteristic disorder of small vessels, if other hazards of diabetes are avoided (Mirsky 1946). Now that these hazards are becoming relatively unimportant, the patient with advancing vascular disease is becoming rapidly more common. That vascular disease, both atherosclerosis and capillary damage, is more common in diabetics than in non-diabetics is the finding of all substantial inquiries both in living and in dead subjects (Liebow et al. 1955, Bell 1950). Capillary lesions are seen with increasing frequency the longer diabetes persists, but atherosclerosis, though abnormally common, seems not to be related to the duration of diabetes (Mirsky 1946).

Atherosclerosis and diabetic "angiopathy," as Lundbæk (1954) has named the capillary disease of diabetes, may be considered separately; it is not to be assumed too readily that they are unrelated, for we have to remember that the angiopathy can be detected in the retina at a very early stage and in the kidney by inference from examination of the urine, whereas atherosclerosis can only be diagnosed in life by rather gross clinical signs. At present there is no conclusive evidence that the arterial lesions differ from those of patients without diabetes. On the other hand, the picture of diabetic angiopathy is gaining definition. The histological changes in the retina described by Ballantyne and Loewenstein (1943) remain specific for diabetes. Ashton (1951) found similar, though not identical, changes in non-diabetic eyes, but the over-all picture is entirely individual. The same is true of the renal disorder. In view of the tendency of pathologists to disagree, the relation of the nodular lesions in the glomeruli to diabetes has been accepted to a remarkable extent (Bell 1950). Apart from other resemblances, the staining reactions of the hyaline material with the periodic-acid stain suggest that the lesions in the kidney and the retina are manifestations of a single disorder, and studies of necropsy material (McManus 1950) confirm that they coexist in all fatal cases. It is this angiopathy, believed to be a specific complication of diabetes, which is under consideration for possible relief by adrenalectomy. Perhaps the lesions occur elsewhere than in the retina and kidney, but it is in these sites that arise the symptoms which justify a desperate remedy. To make a firm criterion for such an interference it is necessary first to consider the clinical course of retinopathy and nephropathy in the absence of specific treatment.

Course of Retinopathy

The ophthalmoscopic picture of diabetic retinopathy, first described with any accuracy by Hirschberg (1890), was classified by Ballantyne (1946) on the basis of many histological examinations. The evolution from the earliest changes (micro-aneurysms) to the final destruction of the

retina, which he described, is now generally accepted, and one may follow his classifications as follows :

(1) Changes chiefly in the central area ; micro-aneurysms with or without punctate hæmorrhages and punctate exudates.

(2) Dot and blot hæmorrhages ; confluent waxy exudates.

(3) Changes in the veins (newly formed intraretinal and preretinal veins ; phlebitis and phlebosclerosis ; and the formation of knots, coils, and loops in the distended veins) ; increasing hæmorrhages in the retina and vitreous ; massive exudates ; retinitis proliferans ; and detachment of the retina.

(4) A further advance in the vessel changes, with increase in vitreous hæmorrhages and exudates, and destruction of the retina.

Little has been written about the duration of these stages and their prognosis, though Ballantyne does not consider them necessarily a sequence of progressive changes. For example, stage 1 may pass directly to stage 3. Ballantyne noted that in stage 1 micro-aneurysms may disappear. Dolger (1947), who believed that the rate of progression of retinopathy was not related to the severity of the diabetes or its control, observed that retinal hæmorrhages often resolved spontaneously, but that retinitis proliferans often progressed to blindness within a year. Work referring to the earlier stages of retinopathy by Wagener (1945), Bartels and Poulsen (1950), Scott (1951), and Vogelius (1949) is concerned mainly with the incidence of retinopathy in diabetic populations. It seems certain that retinopathy will develop in every diabetic who lives long enough, and that the final stage of blindness will arrive in those who do not succumb to renal failure before their sight fails, but the thirty or forty years' follow-up which would show this is not yet possible.

We are here concerned with the tempo of retinopathy and with the prognosis attached to the findings in any given case. In Ballantyne's stage 1 the finding of micro-aneurysms alone may be repeated, without deterioration and even with transient improvement for several years. The longest duration of this stage in my records is nine years. In stage 2 it is usual for the changes to progress within five years to gross visual impairment. Of 19 patients personally observed, in whom the entry into stage 2 could be estimated within six months, 15 were seriously hampered by reduced visual acuity after five years. There are, however, striking exceptions, of which the following is a fair example :

A man developed diabetes at the age of 25. At 43 he complained of poor vision. His visual acuity was corrected to 6/6 in each eye, but stage-2 retinopathy was found. At the age of 48 his visual acuity was corrected only to 6/12 and the retinopathy was more extensive. At the age of 50 his visual acuity was again corrected to 6/6 in each eye and the retinopathy was less obvious.

Usually the younger the patient the greater is the chance of a benign course in stage 2. In stage 3 the visual prognosis is very poor, and cases like the following 2 are quite exceptional :

A woman had diabetes diagnosed at the age of 25 with poor vision and stage-2 retinopathy. At the age of 38 vision of her right eye was suddenly blurred by big vitreous hæmorrhages ; two months later she had a similar episode in her left eye. Both eyes cleared to visual acuity 6/12. She had no further complaint of vision. At the age of 50 she is at work as a housekeeper and can read normal print and sew.

A man developed diabetes at the age of 22. At the age of 34 he was found to have stage-1 retinopathy, but he had no visual impairment until he had a big vitreous hæmorrhage at the age of 47. He had two other hæmorrhages in the same year, and all of them resolved. At the age of 53 his visual acuity is 6/12, and he is working as a bank cashier.

The expectation of useful vision in retinitis proliferans has nowhere been clearly stated. Dolger (1947) emphasised the unpredictable nature of retinopathy and the rapidity with which it may proceed to blindness. Root (1952) reports the duration of retinitis proliferans in 326 cases : in 124 patients who had died the average duration of retinitis proliferans was three years for males and four years for females. Of the 124 deaths 66 were due to renal disease. So far only 25 of the living were known to have become completely blind. Root believes that associated renal or cardiac disease usually leads to death before blindness is complete. This seems to be true, but exceptions are not rare, as in the following cases :

A boy had diabetes at the age of 19 but maintained perfect health until, at the age of 33, he began to have vitreous hæmorrhages, which left him blind at the age of 35. At the age of 41 he remains otherwise well and has no albuminuria.

A woman, who had been treated for diabetes from the age of 30, became blind from retinopathy at the age of 54. She remained otherwise well, with no albuminuria, and died suddenly from coronary thrombosis at the age of 62.

Dolger (1947) found that 50% of his patients had hypertension and 30% albuminuria at the onset of the earliest retinal lesions. Since he did not use mydriatics in examining the eyes he may well have missed minor lesions for a time, with the result that his estimates are perhaps unduly high. In 50 consecutive cases in which the diabetes came on under the age of 50 (as in Dolger's series) with retinopathy but no visual symptoms, the lesions being therefore classified as early, I found hypertension in 26% and albuminuria in 14%. However, with more advanced retinopathy, as Root (1952) has shown, the chances of renal disease are much increased.

Course of Glomerulosclerosis

The first clinical manifestation of glomerulosclerosis is albuminuria. The earliest lesions are almost certainly present for months or years before this finding but remain symptomless, like those in the retina. Under the stress of ketosis an impaired capacity to adjust electrolyte balance may occasionally be noted as evidence of renal damage before albuminuria is found on routine examination. The albuminuria is at first intermittent ; this has been so in every one of the 17 cases observed throughout the course of the disease by me and is noted by Wilson et al. (1951).

The later syndrome is subject to some disagreement : Kimmelstiel and Wilson's (1936) first patients had hypertension, massive œdema, heavy albuminuria, and renal insufficiency ; and several workers (Kimmelstiel and Wilson 1936, Newburger and Peters 1939, Mauser et al. 1942) subsequently correlated this clinical picture with the histological findings of glomerulosclerosis, though the lesions were noted by some workers to be much more common than the syndrome. Henderson et al. (1947) listed, as the clinical features, a long duration of the diabetes, hypertension, albuminuria, renal insufficiency, and mixed diabetic and hypertensive retinopathy. The œdema was omitted. In my 17 cases both pictures have been seen, but œdema appeared during the course of the illness in 14 ; the 3 other patients died of coronary-artery disease, perhaps before the stage of œdema. On the other hand, it must be admitted that some patients with glomerulosclerosis may have escaped diagnosis because of the presence of renal infection or because of there being no necropsy. The inconsistencies in description of the clinical features seem to be mainly due to difference in the patients' ages : the nephrotic picture predominates in the young ; whereas in the elderly there may be no distinctive signs, though diffuse changes are found post mortem.

Once again we are here concerned mainly with the prognostic significance of the clinical features. It seems clear that the appearance of albuminuria in a patient with long-standing diabetes, unless it can be attributed to active urinary infection or to gross cardiac insufficiency, indicates the onset of glomerulosclerosis. Chronic pyelonephritis with secondary hypertension may confuse

the diagnosis, but glomerulosclerosis may accompany this disorder (Rifkin et al. 1952). The term "nephropathy" is preferred by Wilson et al. (1951) because of the difficulty in making this distinction. The finding of doubly refractile lipoid casts in the urine is the most characteristic sign of glomerulosclerosis, but serial examinations are required, and their presence is not pathognomonic. Recent experience indicates that the overwhelming majority of diabetic patients under the age of 50 with chronic renal disease have glomerulosclerosis. In all my 17 cases the diagnosis was confirmed at necropsy, after having been made clinically from the finding of persistent symptomless albuminuria. This is the first clinical manifestation and continues for a variable period before there are added hypertension, impaired renal function, and perhaps œdema. Death takes place from renal failure or less often from congestive cardiac failure: in fact, these conditions usually coincide in the terminal phase.

Glomerulosclerosis is a progressive condition with a grave prognosis, death taking place in from two to five years. Mann et al. (1949) give an average survival of 6·4 years after the onset of nephrosis in 16 fatal cases of renal disease complicating diabetes, but in 8 of these there was no necropsy. Rifkin et al. (1952) did not feel justified in stating the duration of life, because they could not date the onset exactly. In my series the onset of albuminuria could be dated to within six months because the urine was examined for albumin at each routine attendance. If the first finding of albuminuria, rather than the onset of nephrosis, is taken as the point of onset of glomerulosclerosis, the average survival in the 17 cases was 5·2 years.

Indications for Adrenalectomy

If we accept the view that the vascular disease of diabetes is progressive and will ultimately lead to disablement and death, and that adrenalectomy is worth considering as a possible means of arresting this process, we are confronted with a most awkward problem when we come to select the suitable case. The earliest detectable lesions (in the retina) may remain stationary for years, and only an extreme enthusiast would consider so drastic an operation as adrenalectomy at this stage. On the other hand, the later stage of retinitis proliferans or of renal insufficiency is almost certainly beyond the possibility of reversal by any form of treatment. We have to hit on a period when we can say with reasonable certainty that the vascular disease has reached a point from which it will, if untreated, inevitably progress to blindness or renal failure within five years; yet the damage must not have reached an irreversible stage. Such a period may be brief and implies frequent examination of those in whom vascular disease has been detected.

The positive indications seem to be: (1) retinitis proliferans as soon as diagnosed; and (2) glomerulosclerosis of a degree indicated by the following positive features: albuminuria constantly present for six months; a diastolic blood-pressure above 90 mm. Hg after a week of rest in bed; and diabetic retinopathy. Doubly refractile lipoid casts in the urine strongly support the diagnosis but are not pathognomonic. The same applies to œdema of insidious onset. Negative features are the absence of blood casts from the urine and the absence of urinary infection, but it has to be remembered that such do not absolutely exclude glomerulosclerosis. Either of these indications found alone would justify adrenalectomy.

Contra indications against Adrenalectomy

(1) *Advanced renal disease.*—If the blood-urea level, in the absence of fluid and electrolyte disturbance from vomiting or from uncontrolled diabetes, is persistently above 70 mg. per 100 ml., renal failure is likely to be aggravated by adrenalectomy.

(2) *Retinopathy at Ballantyne's stage 4.*—There are unusual cases in which episodes of repeated vitreous hæmorrhage are succeeded by years of adequate vision, and others, more rare, in which renal damage seems to remain stationary for several years; but the overwhelming majority of diabetics with capillary lesions tend to deteriorate progressively. If good functional results are to be achieved, the risk of treating an occasional patient unnecessarily may have to be taken and the decision to intervene reserved for relatively early lesions. It would be easier to convince our patients and ourselves that this decision is right, if evidence of arrest of vascular damage over a substantial time by adrenalectomy could be brought forward. At present the apparent successes are not outside the range of spontaneous remission. It can at least be said that total adrenalectomy is safe, and that the postoperative mainfenance of the patient need not be a burden. A life as tolerable as that before operation is possible, and control of the diabetes will be no less easy.

Summary

Total adrenalectomy was undertaken for vascular disease in 6 diabetic patients. Retinopathy was the indication in all the cases. The follow-up period was from five to sixteen months.

1 patient, already uræmic, died of renal failure two weeks after the operation. In the remainder the operation was uneventful. Retinopathy was improved in 1, unchanged in 3, and worse in 1. Albuminuria was unchanged in the 2 patients in whom it was found before the operation.

Control of the diabetes was unchanged.

The general health was better in 1 patient and unchanged in 4.

The main indications, if any, for adrenalectomy are retinitis proliferans as soon as it is diagnosed and persistent albuminuria in the absence of urinary infection.

I should like to thank Dr. F. E. Higgins, who was largely responsible for the care of these patients at the time of operation, and Mr. J. A. C. Edwards for carrying out the operations faultlessly.

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TRICUSPID VALVOTOMY

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DISEASE of the tricuspid valve is found in 22–36% of cases of rheumatic heart-disease that come to necropsy but is severe in only 9–14% (Cooke and White 1941, Garvin 1943, Smith and Levine 1942), and severe tricuspid stenosis is found clinically in 3·3% of cases of mitral stenosis (Wood 1954).

Tight tricuspid stenosis can give rise to serious disability, with limitation of exercise tolerance by fatigue and angina, and in these circumstances relief of the stenosis is clearly desirable. Tricuspid valvotomy has in fact been done in 18 published cases. It follows from

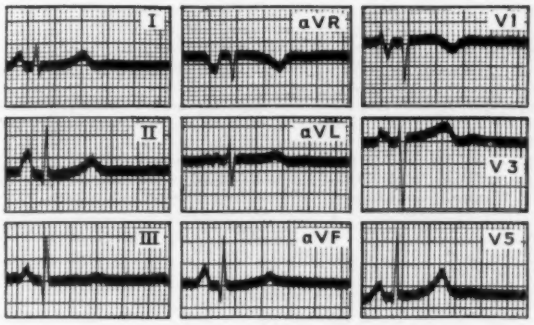

Fig. 1—Electrocardiogram showing P pulmonale (II), P mitrale (V3), deep Q (aVF), and normal ventricular balance.

the known low incidence of severe tricuspid stenosis that this operation is likely to be done relatively infrequently. I report here a case in which mitral and tricuspid valvotomy was done, review the published cases of tricuspid valvotomy, and discuss the problems that arise in relation to the operation.

Case-report

A married woman, aged 24, complained of dyspnœa on exertion and of fatigue for five years, angina for four years, and ankle swelling for three years. These symptoms had progressively worsened until she could not walk more than 100 yards. Everyday activities fatigued her considerably and were accomplished only by a great effort. There had been no hæmoptyses, emboli, paroxysmal dyspnœa, or rhythm change. She had had doubtful rheumatic fever at the age of 5 years. Her father had died from a coronary occlusion and her mother from kidney trouble.

Physical Examination.—She was well nourished, with no cyanosis or mitral facies. The jugular venous pulse showed a dominant *a* wave 6 cm. above the sternal angle. The arterial pulse was of small volume, the blood-pressure was 130/70 mm. Hg, and the hands were cool. The apex-beat was of normal quality, and there was no parasternal lift. At the apex there were a loud presystolic murmur and a loud first sound, no systolic murmur, a soft opening snap, and a fairly long, low-pitched diastolic murmur of moderate intensity. At the left 4th space the signs were very similar, except that with inspiration the presystolic and diastolic murmurs became much louder and longer. An early blowing diastolic murmur was heard at the left 3rd and right 2nd spaces, and an opening snap too at the latter area. The second heart sound was normal.

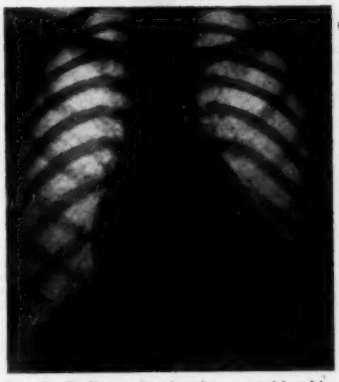

Fig. 2—Radiograph showing considerably dilated right atrium.

Investigations.—Electrocardiography showed a 4-mm. P pulmonale in lead II and a moderate P mitrale in V_3, with a normal ventricular balance. There was a deep Q in aVF (fig. 1). Radiography showed considerable cardiac enlargement (cardiothoracic ratio 65%) with well-marked enlargement of the right atrium and moderate enlargement of the left atrium (fig. 2). No valvular calcification was seen. Cardiac catheterisation (see table) revealed a tricuspid gradient of 10 mm. Hg in atrial systole and 4 mm. Hg in diastole (fig. 3). The *a* wave in the right atrium measured 11 mm. Hg. The pulmonary capillary venous (P.C.V.) pressure of 11 mm. Hg in the presence of a low cardiac output of 3·19 litres a minute suggested tight mitral stenosis, as did the Ry/V of 0·9 (Owen and Wood 1954). Pulmonary stenosis was absent.

Diagnosis.—The clinical diagnosis was mitral stenosis, tricuspid stenosis, and aortic incompetence. The mitral stenosis was considered clinically to be fairly severe on the basis of a long diastolic murmur and a moderate P mitrale.

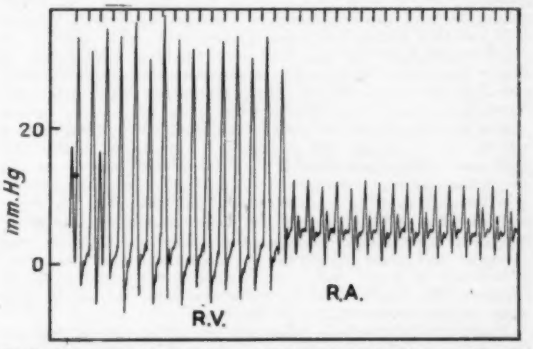

Fig. 3—Cardiac catheterisation: withdrawal tracing from right ventricle to right atrium, showing tricuspid diastolic pressure gradient of 4 mm. Hg (time in seconds).

RESULTS OF CARDIAC CATHETERISATION BEFORE AND AFTER MITRAL AND TRICUSPID VALVOTOMIES

—	Rt aur.	Rt vent.	Pulm. art.	P.C.V.	Cardiac output (litres per min.)	A-V O_2 diff.	Tricuspid gradient		Mitral Ry/V
							Systole	Diastole	
Before	11/5(6)	24/0	24/10(14)	15/6(11)	3·2	6·12	10	4	0·9
After	9/2(5)	21/0	20/7 (12)	12/8(9)	4·0	5·00	6	2	1·38

Pressures in mm. Hg. Mean pressures in parentheses.

The evidence for tricuspid stenosis was the large *a* wave in the absence of any signs of a high pulmonary arteriolar resistance, and the tricuspid diastolic murmurs. Both lesions were confirmed at cardiac catheterisation and shown to be severe. It was decided to undertake mitral valvotomy and, if this afforded no relief of symptoms, to proceed with tricuspid valvotomy at a later date.

Mitral Valvotomy.—Tight mitral stenosis was found, the valve orifice being 1 cm. long; there was no incompetence. It was necessary to cut both commissures, and each was split by about 1 cm. thus producing moderate enlargement of the orifice. Slight mitral incompetence was produced. A striking feature, contrasting strongly with all other cases of mitral stenosis operated on here, was the normal size of the pulmonary artery. Since the stenosis was severe, this was considered to provide good evidence, as did the absence of an opening snap over the valve at operation, that the pulmonary flow was greatly limited by the tricuspid stenosis.

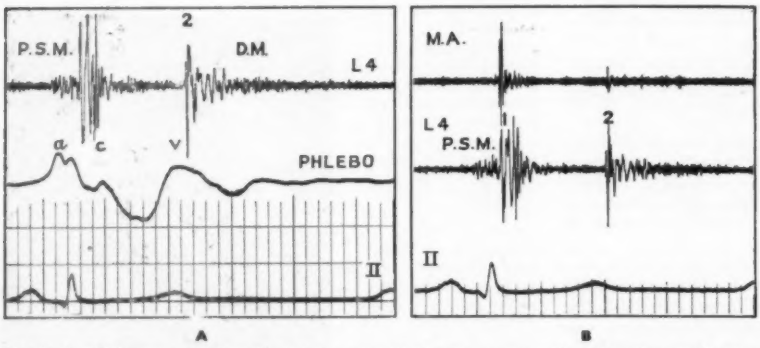

Fig. 4—A, phlebogram showing dominant *a* wave in jugular venous pulse; B, phonocardiograms from mitral area and left 4th space, showing absence of mitral murmurs after mitral valvotomy.

Postoperative Course.—This was uneventful apart from a short attack of precordial pain, probably due to pericarditis, on the tenth day.

Follow-up.—Six months after valvotomy the patient was slightly improved but still had severe effort intolerance, being able to walk only 200 yards. She was now, very interestingly, limited mainly by angina, the dyspnœa (due to pulmonary venous congestion) having been diminished by the mitral valvotomy. Auscultation showed that the apical presystolic murmur and opening snap were now absent and the first sound was softer (fig. 4). A fairly loud opening snap, presumably from the tricuspid valve, was recorded graphically from the left 4th space during inspiration (fig. 5) but was not detected clinically. During the next six months the angina became more severe, bringing the patient to a halt after walking only 50 yards on the flat, and sometimes being present at rest. Electrocardiography after effort showed ischæmic changes (ST depression).

Tricuspid valvotomy was done a year after the mitral valvotomy. The cavity of the right atrium was very large. The tricuspid orifice was small, being just under 1 cm. long; palpation gave the impression of a round opening in a fairly thin resilient membrane moving very little with systole. A small regurgitant jet was felt near the posterior wall. A finger was thrust through the opening without any difficulty, and the valve was felt to split, apparently posterolaterally. Some ballooning of the anterior part of the valve could be felt which was comparable to that in the aortic cusp of a stenosed mitral valve, though not nearly so pronounced. After the split the orifice measured 3 × 1·5 cm. and was 7 cm. in circumference, and a definite increase in the regurgitant stream was felt. A systolic thrill was now palpable over the right atrium. The atrium was less distended, its surface appearing wrinkled instead of smooth, and atrial contraction was stronger and more effective. On direct auscultation before valvotomy a fairly long and rather low-pitched diastolic murmur was heard over the right ventricle, but an opening snap was not detected.

Postoperative Course.—After the operation the patient got up on the third day and was discharged on the eighteenth day; there were no complications. After tricuspid valvotomy there was a dramatic symptomatic improvement; the anginal pain completely disappeared even on exertion, whereas before operation it occurred daily while the patient was at rest in bed in hospital. The patient was, however, still limited by breathlessness and could only walk slowly about half a mile on the flat; stairs were managed if taken slowly. On examination there was still a prominent though diminished 4-cm. *a* wave in the neck. The tricuspid diastolic murmurs were still present, and the tricuspid opening snap was still recorded on the phonocardiogram. In addition a soft tricuspid systolic murmur had appeared since the valvotomy. The aortic diastolic murmur was unchanged.

Cardiac catheterisation three months after tricuspid valvotomy showed that the tricuspid gradient had been diminished in atrial systole from 10 to 6 mm. Hg and in diastole from 4 to 2 mm. Hg. Since the cardiac output had risen by 25% between the two observations, the reduction of the gradient by about 50% is undoubtedly significant. The P.C.V. pressure of 9 mm. Hg was slightly less than the figure of 11 mm. Hg obtained before mitral valvotomy, as was the degree of obstruction at the mitral valve measured by the Ry/V of 1·38 compared with 0·9. Some degree of mitral stenosis is present, accounting for the breathlessness still experienced.

Discussion

Cossio and Perianes (1949) described the production of incompetence of the normal tricuspid valve by passing an instrument through the jugular vein for the relief of chronic pulmonary congestion. Surgical relief of rheumatic tricuspid stenosis was first reported by Brofman (1953), and since then, including the present case, 19 cases have been published, with no operative deaths (Bailey 1955, Chesterman and Whitaker 1954, Dogliotti 1954, Krook et al. 1955, O'Neill et al. 1954, Rubio and Lason 1954, Swan et al. 1955, Trace et al. 1954).

The sex ratio was 7 women to 2 men in the 9 cases in which the sex was stated, with an age range of 21–43 (mean 29). The mean age at mitral valvotomy is 36·8 years (Wood 1954). This accords with the finding of Thompson and Levine (1937) that the average age at onset of symptoms in rheumatic heart-disease is earlier when tricuspid stenosis is present. Of the 19 cases, the diameter of the tricuspid valve orifice was 5–13 mm. in 5, and was described as tight in 3 others and moderate in 1, no details being given of the remainder. The shape was triangular, circular, or slit-like. In some cases, as in the present one and that of Chesterman and Whitaker (1954), the valve orifice appeared as a circular opening in a smooth diaphragm, and it was impossible to feel the individual commissures. In others it is stated or implied that one or more of the commissures could be detected. Calcification in the valve has not been reported.

A direct approach to the valve was used by all except Rubio (Rubio and Lason 1954), who uses a cutting wire in the end of a ureteric catheter. Most workers have found that instrumental division of the valve was often required, although none states that valvotomy was especially difficult.

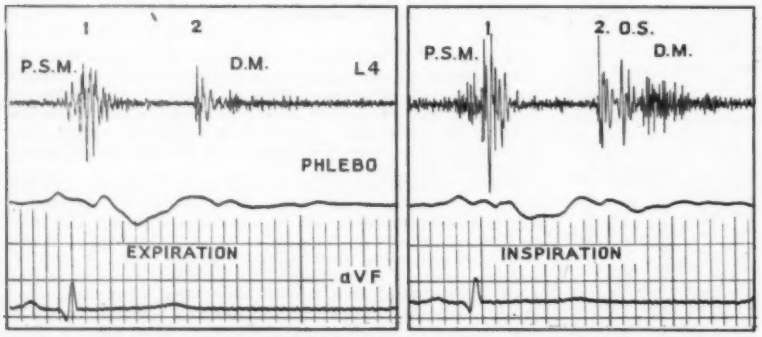

Fig. 5—Phonocardiograms from left 4th space, showing increase in intensity of diastolic murmurs on inspiration, and emergence of opening snap (O.S.).

Bailey (1955) points out that subvalvular fusion is much less common in the tricuspid than in the mitral valve; so this cause of difficulty, found with mitral valvotomy, should be absent from tricuspid valvotomy.

In the 4 cases where details were given, each of the three commissures was divided with equal frequency: in 2, two commissures were divided; and in 2, one commissure was divided. In the present case the valve split naturally along the posteroseptal commissure, and in the other cases particular commissures were deliberately incised. Bailey (1955) states that division of the anteroseptal commissure is to be avoided because it weakens the tricuspid valve "baffle" and is therefore likely to cause incompetence.

A significant degree of enlargement was produced in all the published cases, the final valve orifice admitting $1^1/_2$–2 fingers or measuring 3·0–3·5 cm. long. The tricuspid-pressure gradient was measured before and after operation by cardiac catheterisation in 3 cases, including the present one, and it was reduced by 1, 3, and 6 mm. Hg.

Tricuspid incompetence is often found in tricuspid-valve surgery. Anatomical study of diseased tricuspid valves led me to think that incompetence was likely to be a usual accompaniment of stenosis and to be found more frequently than with mitral stenosis, even when the tricuspid stenosis was tight (Hollman 1956). Incompetence was absent in only 2 of the 8 surgical cases in which this point was specifically mentioned. After valvotomy moderate incompetence was produced in 1 case in which it had been previously absent; but where incompetence was already present it was increased in only 1 case (the present one). I know, from personal communications on 2 unpublished cases, that severe incompetence, in 1 case fatal, was produced at tricuspid valvotomy; it therefore seems important to avoid producing serious incompetence even if, as in the present case, this means only partial relief of stenosis.

Associated Valve Disease.—Severe mitral stenosis commonly coexists with tricuspid stenosis (Lewis 1946), and mitral valvotomy was done in all the published cases of tricuspid valvotomy except 1 (Krook et al. 1955). When both valves are dealt with at one operation, a sternum-splitting approach is advised (Bailey 1955). Severe tricuspid stenosis limits the mitral blood-flow and therefore decreases the symptoms and signs of mitral stenosis. It may be difficult to judge the severity of the mitral lesion in these circumstances, but cardiac catheterisation will prove the severity, and it is wise to assume that mitral stenosis, if present, is tight unless proved otherwise. It is logical to do the mitral valvotomy first, lest pulmonary œdema develop on relief of the tricuspid stenosis. Disease of the aortic valve is often associated with tricuspid stenosis—in 35% of cases according to Osler and McCrae (1927). In none of the reported cases of tricuspid valvotomy, including the present one, was there serious aortic disease, but this may have been due to deliberate selection.

Signs and Symptoms of Tricuspid Stenosis.—Tricuspid stenosis is diagnosed clinically by observing a giant *a* wave in the jugular venous pulse in the absence of signs of a very high pulmonary arteriolar resistance (Gibson and Wood 1955). The diagnosis is confirmed by finding, over the tricuspid area, presystolic and diastolic murmurs which are intensified during inspiration; and, according to Likoff (Bailey 1955), by turning the patient on to his right side; and occasionally by finding a tricuspid opening snap, as in the present case, brought out by inspiration. The symptoms of tricuspid stenosis are presumably due to limitation of cardiac output, with corresponding diminution in pulmonary venous congestion; fatigue and angina are thus prominent. That these symptoms may be properly ascribed to tricuspid involvement is well shown in the present case, where mitral valvotomy relieved the dyspnœa, leaving angina as the dominant complaint, which in its turn was relieved by tricuspid valvotomy.

Summary

The case is described of a woman, aged 24, with mitral and tricuspid stenosis; the dominant symptom of the tricuspid stenosis was angina pectoris. Tricuspid and mitral valvotomy was successfully undertaken, and partial relief of the tricuspid stenosis gave considerable symptomatic benefit.

Among 18 reported cases of tricuspid valvotomy there were no deaths.

Tricuspid incompetence is commonly associated with stenosis, even when this is tight, and it is important to avoid producing serious incompetence at operation. For this reason only a limited valvotomy may be possible.

It is a pleasure to thank, for their encouragement and advice, Dr. Kenneth E. Harris, under whose care the patient was, and Prof. R. S. Pilcher who performed the valvotomies.

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TREATMENT OF HAY-FEVER WITH HYDROCORTISONE SNUFF

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IT is well known that hydrocortisone, in contrast to cortisone, will relieve certain disorders of the skin when applied locally. It has also been used locally in chronic allergic rhinitis with some success by several workers: Tuff (1954) used a hydrocortisone suspension combined with two vasoconstrictor substances acting as nasal decongestants; Rohen (1955) and Burger and Shaffer (1955) used a pure hydrocortisone suspension; and Foulds et al. (1955) used hydrocortisone powder as a snuff.

We present here the results obtained by treating 24 cases of pollen hay-fever with hydrocortisone acetate in the form of a fine powder applied locally to the nasal mucosa.

Method

The patients, 10 females and 14 males, aged 14–35, were chosen because of the severity of their symptoms and their lack of response to previous treatment, including treatment with anti-histamine substances to the limit of tolerance. All gave a typical history of two years or more of continuous severe hay-fever during the summer months only. All had a positive skin reaction to mixed grass pollens. No case had been desensitised to pollen during the previous twelve months.

TABLE I—INITIAL RESPONSE

Case no.	Date of starting treatment with hydrocortisone	Complete freedom from symptoms		No. of days before response
		Nose	Eyes	
Patients taking anti-histamine substances :				
1	May 11	+	+	2
2	May 24	+	+	1
3	June 2	+	+	2
4	June 10	+	+	2
5	June 16	+	+	2
6	June 16	+	—	2
7	June 21	+	+	2
8	June 22	+	—	7
9	June 23	+	+	1
10	June 23	+	+	2
11	June 24	+	+	2
12	June 29	+	+	2
13	July 5	+	+	9
Patients not taking anti-histamine substances :				
14	May 14	+	+	2
15	May 24	+	+	2
16	May 27	+	+	1
17	May 31	+	+	2
18	June 2	+	+	2
19	June 2	+	+	3
20	June 10	—	—	..
21	June 16	+	—	3
22	June 16	+	+	1
23	June 30	+	+	1
24	July 1	+	+	7
Total responding		23	20	

Hydrocortisone powder was used rather than the suspension, because in this way the substance reaching the mucosal surface is undiluted, non-irritant, and retained in the nose more easily. The powder, which was ground very finely * was supplied in 100-mg. capsules containing 15 mg. of hydrocortisone acetate and 85 mg. of lactose. The capsules were pierced at the upper end and placed in a nasal insufflator from which a fine spray was produced. This spray was applied to both nostrils three times a day, the whole 15 mg. being used in twenty-four hours.

In many cases the initial blockage of the nose by the hay-fever made it necessary to create an airway to allow the powder to reach the nasal mucosa. These patients were therefore asked to instil into both nostrils one or two drops of 0·02% naphazoline ('Privine') to unblock the nose. When the naphazoline had freed the airway, the hydrocortisone powder was inhaled, and this pre-treatment with naphazoline was discontinued when the airway remained clear (in most cases after two days).

The hydrocortisone inhalations were kept up for five days and then omitted to see if relapse occurred, but further hydrocortisone was given if and when symptoms recurred. Those patients in whom a partial control of symptoms had previously been obtained by anti-histamine substances continued with the same drug and dosage throughout in addition to the hydrocortisone.

Results

No side-effects of any kind were observed during the treatment. The powder was applied without difficulty once the patients had mastered the fact that it was useless to apply it to a blocked or watering nose. With perseverance every patient except 1 (case 20) was able to free the nose temporarily with the naphazoline before applying the powder. In no case was local irritation of the nose produced by the powder.

The initial response to hydrocortisone was excellent (table I). All the patients but 1 obtained relief from nasal symptoms within ten days, and most of them responded dramatically within forty-eight hours. The slower responses were in those patients who had profuse rhinorrhœa preventing the powder from being retained in more than small quantities.

* The particle size was not determined accurately. An approximate survey indicated a mean diameter of 5 μ.

The later results were also very encouraging (table II). 19 patients were followed up for the whole season, and only 2 of these relapsed while taking hydrocortisone. 9 of the successful patients had to take the powder until the end of the pollen season but had perfect control of their symptoms all the time they were taking it. After the first five days' treatment most of these patients did not relapse immediately when the drug was withdrawn but remained free from symptoms for up to sixteen days. When hydrocortisone was resumed, they responded and remained symptom-free for as long as they were taking it. In the remaining 8 successful cases the patients discontinued hydrocortisone permanently after five to twenty days and remained satisfactorily controlled thereafter. These patients tended to have a return of minimal symptoms but to a degree so slight as not to justify taking further hydrocortisone. 6 of these 8 patients were on anti-histamine substances and continued with them after stopping hydrocortisone.

An unexpected and remarkable result was seen in the effect of hydrocortisone on the eye symptoms associated with rhinitis initially in all cases. Itching and watering of the eyes and accompanying conjunctival injection disappeared in 20 of the 24 patients during their initial response. A further point of interest was the behaviour of the 10 patients who previously had had pollen asthma every year in addition to hay-fever. In 4 of them no chest symptoms developed, all being patients taking hydrocortisone to the end of the season. It is likely that in these cases the part of the hydrocortisone which penetrated into the bronchi had a curative effect, as has been observed by Foulds et al. (1955). The remaining 6 patients had their asthma as usual.

There was no significant difference in the results between the group taking anti-histamine substances and the others.

Discussion

The initial response to this form of local hydrocortisone treatment was dramatic. As could be expected, relapse occurred in some cases as soon as the treatment

TABLE II—LATE RESULTS

Case no.	Date of starting treatment with hydrocortisone	No. of days' treatment	Whole season control		Degree of freedom from symptoms
			Nose	Eyes	
Patients taking anti-histamine substances :					
1	May 11	Whole season	+	+	Complete
2	May 24	Whole season	+	+	Complete
3	June 2	15	+	+	Complete
4	June 10	5	+	+	Complete
5	June 16	Whole season	+	+	Complete
6	June 16	10	+	—	Almost complete
7	June 21	5	Not followed up		..
8	June 22	20	+	—	Almost complete
9	June 23	Whole season	+	+	Complete
10	June 23	10	+	+	Only fair
11	June 24	5	Not followed up *		..
12	June 29	5	+	+	Almost complete
13	July 5	Whole season	+	+	Complete
Patients not taking anti-histamine substances :					
14	May 14	5	Not followed up *		..
15	May 24	15	+	+	Complete
16	May 27	10	+	+	Complete
17	May 31	Whole season	+	+	Complete
18	June 2	15	—	—	Relapsed
19	June 2	10	—	—	Relapsed
20	June 10	10	Not followed up		No response
21	June 16	5	Not followed up		..
22	June 16	Whole season	+	+	Complete
23	June 30	Whole season	+	+	Complete
24	July 1	Whole season	+	+	Almost complete
Total (19 cases followed up)			17	15	12 complete 4 almost complete 3 failures

* Corticotrophin administered because of asthma.

was withdrawn; but all the patients who continued to take it throughout the whole season remained free, or almost free, from symptoms. It is remarkable that 8 patients remained free from symptoms in spite of the withdrawal of treatment, and in spite of the fact that the season had only just started or was at its height. A similar observation was made by Schiller and Lowell (1953). They gave oral cortisone 100 mg. daily to 51 patients for four days. This achieved complete or satisfactory relief in 42 patients, of whom 20 relapsed within a week. The remainder were free from symptoms for the rest of the season. It seems possible that in these cases and in ours a spontaneous partial desensitisation took place under the influence of these drugs. Such desensitisation has been demonstrated experimentally under the cover of systemic cortisone (Herxheimer 1954). When some of our patients relapsed after a long interval of having no hydrocortisone, the time of their relapse did not coincide with any particular high atmospheric pollen count. Possibly they had exposed themselves accidentally so heavily that the allergen broke through the protection given by a moderate degree of desensitisation. In all these cases freedom from symptoms could be restored at once by resumption of the treatment.

It would have been desirable to give a placebo powder during the withdrawal. This would have shown us how many placebo reactors, if any, were in our series. It is, however, unlikely that our very high proportion of successes could have been produced by psychological factors. Moreover our patients had all had very severe hay-fever for several or many years and were very sceptical of this new treatment after the lack of success of previous efforts to relieve their symptoms. The number of placebo reactors in our series can therefore be expected to be small. We have been unable to observe a control series, because our supply of suitable patients with severe and uncontrollable hay-fever was limited, and we did not wish to reduce our small series further.

The method of treatment described here has one great advantage over desensitisation therapy in that it is safe. Hydrocortisone powder in a dose of 15 mg. daily applied locally to the nose for a maximum of eight weeks could not have any harmful effect even if most of it is absorbed.

Hay-fever, in severe cases, gives rise to much discomfort and disability, and any simple and safe method of treating it is welcomed by patients. The subjects of this trial have been full of enthusiasm for the method, many of them stating that this was the first summer for many years they had been able to enjoy. Our experience in this small series indicates that the method is worthy of a wider trial during the next pollen season.

Summary

In 23 of 24 patients with severe hay-fever who were given 15 mg. of hydrocortisone snuff daily, complete control of symptoms was achieved during the first two weeks' treatment.

In 17 of the 19 cases which could be followed up for the whole season satisfactory control of symptoms was achieved throughout.

Of the 19 patients followed up 8 discontinued the hydrocortisone within three weeks and did not relapse thereafter.

We are indebted to Messrs. Upjohn of England for the supply of hydrocortisone powder and powder inhalers, and to Miss P. McInroy for technical and other assistance.

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RADCLIFFE RESPIRATION PUMPS

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ARTIFICIAL respiration by intermittent positive pressure (I.P.P.R.) through a cuffed tracheotomy tube was introduced by Lassen and Ibsen (Lassen 1953) for treating respiratory insufficiency in poliomyelitis. This way of giving artificial respiration has proved, in competent hands, the method of choice when the throat as well as the muscles of respiration is paralysed. Thus I.P.P.R. has proved invaluable in combined bulbar and spinal poliomyelitis and in conditions such as polyneuritis and tetanus (during curarisation).

Various machines have been devised to provide a respiration pump for this purpose. The apparatus described here has been developed from the Radcliffe respiration pump, type A, devised by Russell and Schuster (1953). As in the original pump, the positive-pressure wave is effected by the free pressure of a weight on bellows. This has proved the best method we know of, for it removes all need for safety blow-off valves and gives a square wave form which provides the maximum of ventilation in the shortest time, and so imposes the minimum of strain on the circulation (Spalding and Young 1955). Further, the visible movement enables the nurse in charge to recognise any abnormality in the speed at which the bellows falls.

The original pump has been greatly improved by the manufacturers (Messrs. H. G. East & Co.) and has proved in practice a reliable machine capable of operating continuously for many months with very little maintenance. The use of a Sturmey-Archer bicycle gear-box provides a wide range of speeds at small cost and very little noise. The Stott flutter valve (Smith et al. 1954) continues to operate well, even when water has condensed in it, and its snoring sound provides an audible check of the volume of expired air with each breath. The expired air can be measured with a gas-meter as it emerges from the valve. The whole apparatus, complete with humidifier (Marshall and Spalding 1953) and gas-meter, is shown in fig. 1. The apparatus incorporates both a 230-volt A.C. and a 12-volt D.C. motor, which provide both for continuous use in hospital and for battery operation in the case of transport by road or air.

Radcliffe Positive-negative Pressure Respiration Pump

The clinical results obtained by pumps of the type shown in fig. 1 cannot easily be bettered (Smith and Spalding 1955), but some physiologists argue that a negative-pressure phase is desirable in expiration to facilitate the venous return to the right heart. This has therefore been incorporated in the newest design, which is therefore called the Radcliffe positive-negative pressure respiration pump (figs. 2–4). Cam-operated valves have also been introduced as being more reliable than pressure-operated valves. The negative-pressure phase, like the positive-pressure phase, is gravity-operated and designed to provide negative pressure from 0 to −10 cm. water. Other features are as follows:

Alternative Motors.—The apparatus incorporates both a 230-v. A.C. and a 12-v. D.C. motor. The latter is convenient for travelling or in case of prolonged electrical failure.

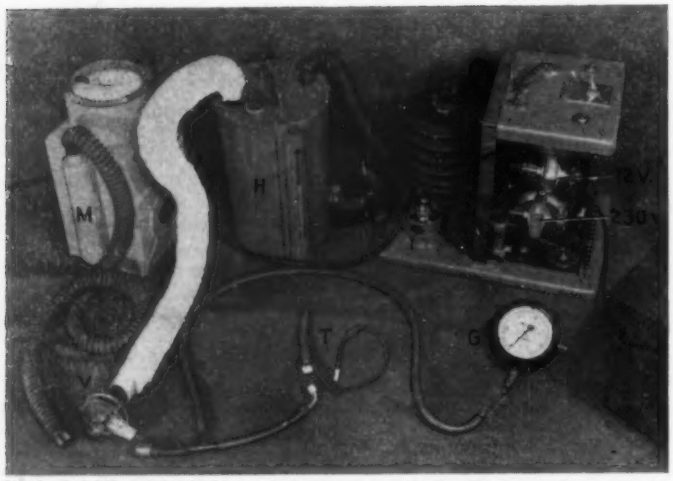

Fig. 1—Radcliffe respiration pump in its most used form. The items shown are the bellows (P), humidifier (H), Stott valve (V), tracheotomy tube (T), gas-meter (M), pressure gauge (G), and 12-volt D.C. and 230-volt A.C. motors.

Simple and Easy Hand Operation.—A handle is inserted and turned at the appropriate speed. No clutch is required to disconnect the motor, because there is a free-wheel in the gear-box, and the weight-controlled wave-form and pressure of delivery remain entirely uninfluenced by the operator's actions.

Respiratory-rate Control.—For use with adults respiratory rates of 12, 16, 20, and 25 are available. For young children an alternative sprocket is used in the drive to provide respiratory rates of 20, 23, 30, and 37.

Oxygen Intake.—Though oxygen is rarely used for these cases, a simple system is available whereby the continuous flow of oxygen from a cylinder meets the intermittent requirements of the positive-pressure bellows, any required mixture of air and oxygen being easily provided. This consists of a length of corrugated breathing-tube, of which one end is open to the air and the other is attached to the pump intake. Oxygen is led in at the pump end of this tube so that it accumulates in the tube to form a reservoir for each intake. This device is seen below the bellows (P) in fig. 2.

Figs. 2-4—Radcliffe positive-negative respiration pump (side plates removed) showing main components: positive-pressure bellows (P), negative-pressure bellows (N), humidifier (H), cam-operated valves (V), gas-meter (M), and 12-volt D.C. and 230-volt A.C. motors.

Positive-pressure control providing pressure from +10 to +30 cm. water.

Humidifier gauge showing the amount of water in the humidifier.

Pressure Gauges.—There are two pressure gauges, one reading from the inspiratory valve, the other from close to the patient. Water traps are included to insure that water cannot reach and block the gauges.

Removable trap in which secretions contained in the expired air are collected.

A *gas-meter* is incorporated and is switched in or out of the expiratory side of the circuit at will.

Negative-pressure control providing pressure from 0 to −10 cm. water.

Safety devices include a rod attached to each bellows (R in fig. 2) and providing a visible indication of the bellows' action. An audible and visible warning device will also be incorporated because the snore of the Stott valve has in practice proved a most effective safety device which is lost with cam-operation of the valves. The readings on the pressure gauges and gas-meter provide additional safeguards, and if the patient can coöperate he can be provided with foot-operated or chin-operated switch for an electric bell.

The complete apparatus is mounted on a trolley measuring 2 ft. 6 in. × 1 ft. 8 in. × 2 ft. 6 in. The trolley includes a folding shelf and an arm to support the tubes going to and from the patient. Extra apparatus—e.g., throat

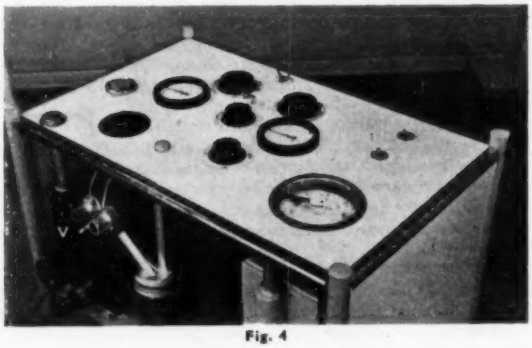

Fig. 4

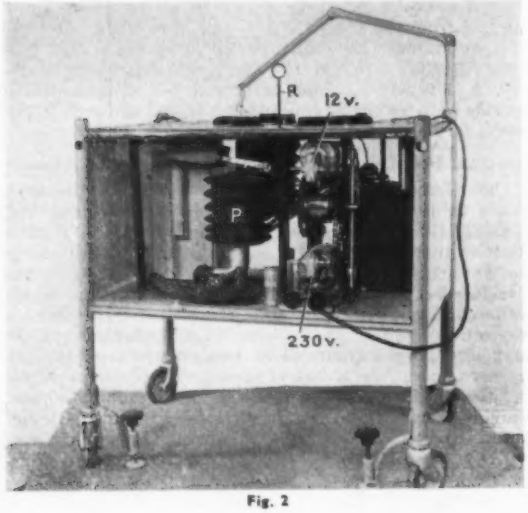

Fig. 2

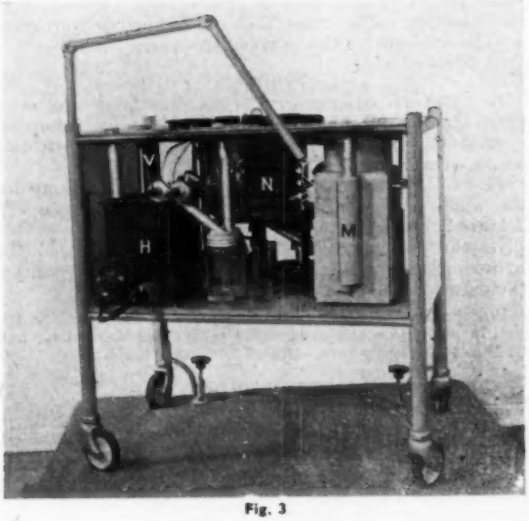

Fig. 3

microphone, oximeter, and CO_2-meter—can be added to the trolley if required.

The pump is illustrated in figs. 2–4 with the side plates removed. Fig. 5 shows the type of wave form obtained with the pump on a patient, and it is seen that the square wave form appears in both the positive-pressure and the negative-pressure phases.

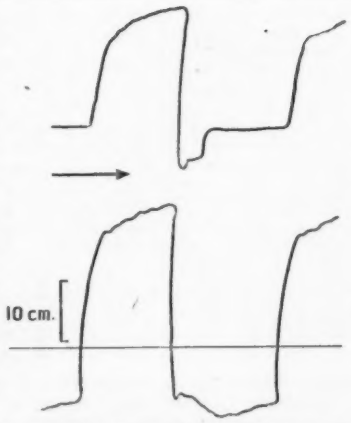

Fig. 5—Wave forms obtained with positive-negative pressure pump, with partial negative pressure and full negative pressure.

Summary

Radcliffe respiration pumps have proved most successful in the treatment of combined respiratory and bulbar paralysis.

A development of the original pump is described which includes a negative-pressure phase.

The design of this second type of pump has also been much improved by the manufacturers (Messrs. H. G. East & Co., 37a, Oxford Road, Cowley, Oxford), to whom we are greatly indebted.

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DELAYED PROTHROMBIN ESTIMATION IN OUTPATIENT ANTICOAGULANT THERAPY

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PROLONGED anticoagulant therapy continued over months or years must of necessity be conducted on an outpatient basis. Laboratory control is essential, and patients have to report at short intervals to a hospital with laboratory facilities for accurate prothrombin-time estimations and where the medical staff is skilled and experienced in the control of such treatment. This has proved difficult where patients are either fully employed or cannot travel easily, and has led to loss of work and frequent use of the ambulance service. Further, the maintenance of anticoagulant therapy is restricted to patients living where these facilities exist.

Freshly withdrawn samples of venous blood are requested by laboratories for the one-stage prothrombin test, and this, so far as can be ascertained, is common practice. It is generally stated that the specimen deteriorates fairly rapidly; and Quick (1951), describing the test, states that, though the estimation should be made within 30 minutes in research studies, up to 4 hours' storage is permissible for routine clinical purposes.

Since the necessity for rapid estimation appeared to be a major factor in the problem outlined above, it was decided to put it to the test by making a pilot study of prothrombin-times estimated 24 hours after withdrawal of the samples of blood. This work was done in 1953 as part of a larger investigation, and the present report is prompted by the imminence of large-scale clinical trials of prolonged anticoagulant therapy.

It should be emphasised that the prothrombin-time estimations were not made as a research study but were made each morning in the laboratory with large batches in the usual routine way. Certain precautions were taken, however, to ensure that the identity of the specimens was unknown to the technician making the estimations.

Method and Results

The one-stage prothrombin test was used with fresh human brain as the source of thromboplastin. A fresh thromboplastin solution was prepared and a control specimen estimated each morning. The samples of blood were obtained by clean venepuncture, 4·5 ml. of venous blood being run into a glass tube containing 0·5 ml. of 1·34% sodium-oxalate solution and carefully mixed. On reaching the laboratory the whole specimen was spun for 10 minutes at 2500 r.p.m., and 0·1 ml. of the plasma thus obtained was used for the estimation. For the purpose of the investigation enough blood was taken at each venepuncture to obtain three specimens:

(1) The first was labelled by the house-physician and sent for estimation in the normal way with many others from the ward or outpatient clinic. It was the specimen used to control the patient's daily dose of coumarin drug.

(2) The second specimen was also sent for immediate estimation under another name.

(3) The third was carefully wrapped and sent through the post addressed to the sender. When it returned to the department 24 hours later it was sent for estimation with that day's specimens under a different name.

As a further check the first two specimens were on several occasions retrieved after estimation, relabelled with different names, and posted in a similar way for estimation the following day. The technician could not

TABLE I—EFFECT ON ONE-STAGE PROTHROMBIN-TIME WHEN WHOLE-BLOOD SPECIMENS ARE KEPT FOR 24 HOURS AT ROOM-TEMPERATURE BEFORE ESTIMATION

Case no.	One-stage prothrombin-times						Error in delayed samples (sec.)*
	On day of withdrawal			24 hr. later			
	Control time (sec.)	Patient's time (sec.)	Activity (%)	Control time (sec.)	Patient's time (sec.)	Activity (%)	
1	14	19	30	14	19	30	0
2	14	25	20	14	25	20	0
3	14	33	14	15	33	16	2
4	14	40	11	15	44	10	0
5	15	35	14	14	33	14	0
6	15	23	24	14	22	24	1
7	14	28	17	14	28	17	0
8	14	33	14	14	34	14	1
9	16	38	15	16	38	15	0
10	15	29	19	15	26	22	3
11	15	29	19	15	28	18	1
12	15	22	28	15	22	28	0
13	15	30	18	15	30	18	0
14	15	38	14	15	38	14	0
15	15	23	27	15	24	25	1
16	14	25	19	14	25	19	0
17	14	20	30	15	22	28	1
18	15	27	18	15	30	17	3
19	15	34	16	15	38	14	4
20	15	33	15	16	34	17	2
21	14	22	22	14	19	30	3
22	14	25	19	14	22	22	3
23	14	34	14	14	34	14	0
24	14	30	17	14	28	18	2
25	14	28	18	14	26	19	2
26	14	28	18	15	30	18	0
27	15	26	22	14	26	19	2
28	15	25	23	15	25	23	0
29	14	32	16	15	34	16	0
30	16	36	16	16	36	16	0

* Where the control times differ, the error has been corrected to the first control time in simple proportion. This is permissible since in the therapeutic range the curve of prothrombin activity is virtually linear.

know which specimen belonged to a given patient, whether it was fresh or 24 hours old, and whether or not it had been already estimated the previous day. The results could only be interpreted when the key to the many names used was consulted. In this way it was possible to check the accuracy of the estimations and to find out what effect 24 hours' delay had on the results.

No statistical study was made, but table I shows that there is a close relationship between the two sets of readings. There are minor variations, partly due to the control time varying on successive days, but in practice either result could have been used to maintain satisfactory control of the treatment.

Further tests were done to find out if there was a difference in the delayed estimation when plasma was used instead of whole blood. The specimen was obtained by spinning the blood immediately after withdrawal and, together with a sample of whole blood, posted as outlined above. The results obtained were once again very similar and are shown in table II, suggesting that the extra trouble and apparatus required to obtain the plasma were unnecessary.

It had previously been suggested (J. A. Tulloch, personal communication) that the best method of obtaining a prothrombin-time, when an immediate test could not be made, was to put the plasma on ice. So an experiment was made exactly as before with the samples of whole blood and plasma duplicated. Two were sent through the post and two were kept in the refrigerator for 24 hours before estimation. Table III shows that there was little difference in the one-stage prothrombin-times, which were again, from a therapeutic point of view, almost identical with those of the sample estimated immediately after withdrawal.

TABLE II—EFFECT ON DELAYED ONE-STAGE PROTHROMBIN-TIME OF PLASMA COMPARED WITH WHOLE-BLOOD

Case no.	Whole blood						Plasma 24 hr. later		
	On day of withdrawal			24 hr. later					
	Control time (sec.)	Patient's time (sec.)	Activity %	Control time (sec.)	Patient's time (sec.)	Activity %	Control time (sec.)	Patient's time (sec.)	Activity %
1	14	34	14	14	34	14	14	34	14
2	14	30	17	14	28	18	14	29	19
3	14	28	18	14	26	19	14	31	15
4	14	28	18	15	30	18	15	30	18
5	15	25	23	15	25	23	15	26	22
6	14	32	16	15	34	16	15	33	16
7	15	29	19	15	26	22	15	30	18
8	15	29	19	15	28	18	15	24	25
9	15	30	18	15	30	18	15	27	20
10	15	38	14	15	38	14	15	34	16
11	15	23	27	15	24	25	15	24	25
12	14	25	19	14	25	19	14	25	19
13	14	20	30	15	22	28	15	21	26
14	15	27	18	15	30	17	15	34	15
15	15	33	15	16	34	17	16	36	16

TABLE IV—EFFECTS ON IMMEDIATE AND DELAYED ONE-STAGE PROTHROMBIN-TIMES WHEN WHOLE BLOOD IS HÆMOLYSED MECHANICALLY

Case no.	Non-hæmolysed						Hæmolysed					
	On day of withdrawal			24 hr. later			On day of withdrawal			24 hr. later		
	Control time (sec.)	Patient's time (sec.)	Activity %	Control time (sec.)	Patient's time (sec.)	Activity %	Control time (sec.)	Patient's time (sec.)	Activity %	Control time (sec.)	Patient's time (sec.)	Activity %
1	15	22	26	15	22	26	15	22	26	15	24	22
2	15	28	18	15	26	20	15	30	17	15	31	32
3	15	24	22	15	26	20	15	25	20	15	26	20
4	16	38	15	16	38	15	16	36	16	16	36	16
5	14	33	14	15	33	16	14	34	13	15	34	15
6	14	25	20	14	25	20	14	26	19	14	26	19

TABLE V—EFFECT ON IMMEDIATE AND DELAYED ONE-STAGE PROTHROMBIN-TIMES WHEN WHOLE BLOOD IS HÆMOLYSED BY ADDITION OF SURGICAL SPIRIT

1	15	35	14	14	33	14	15	43	11	14	40	11
2	15	23	24	14	22	24	15	32	16	14	34	14
3	14	28	17	14	28	17	14	34	14	14	41	10
4	14	33	14	14	34	14	14	39	11	14	29	17
5	15	30	17	14	28	17	15	38	14	14	43	9
6	15	31	16	15	30	17	15	40	12	15	35	14

Finally the effect of hæmolysis was investigated. Many of the routine samples arriving at the laboratory from the wards were hæmolysed, and it was the practice to request a fresh specimen in such cases. In view of this the plasma used in the above-mentioned tests was examined spectroscopically, and any specimen showing more than a faint trace of hæmolysis was discarded from the series.

It was decided to study the effect of deliberate hæmolysis in the duplicate sample. This was found to be very difficult to achieve, at least by mechanical means. High-pressure ejection from the syringe through a small-bore needle followed by vigorous shaking of the tube was successful in a few cases. Hæmolysis produced in this way had no significant effect on either the immediate or the delayed one-stage prothrombin-time (table IV). It was thought probable that contamination by either methylated ether or surgical spirit might be responsible for the hæmolysis commonly seen; so a group was tested in which one drop of surgical spirit had been deliberately added to the duplicate sample. This produced gross hæmolysis in every case, and the close relationship noted between the two sets of results in all previous experiments was no longer found (table V).

Discussion

The care of patients on prolonged anticoagulant therapy involves far more than adjustment of their daily dose of coumarin drug, and their supervision must remain in the hands of experienced physicians. It therefore remains necessary for them to report back to the main

TABLE III—EFFECTS OF ROOM-TEMPERATURE AND OF REFRIGERATION ON DELAYED ONE-STAGE PROTHROMBIN-TIME OF WHOLE BLOOD AND PLASMA

Case no.	Whole blood						Plasma after 24 hr. in post			Whole blood after 24 hr. in refrigerator			Plasma after 24 hr. in refrigerator		
	On day of withdrawal			After 24 hr. in post											
	Control time (sec.)	Patient's time (sec.)	Activity %	Control time (sec.)	Patient's time (sec.)	Activity %	Control time (sec.)	Patient's time (sec.)	Activity %	Control time (sec.)	Patient's time (sec.)	Activity %	Control time (sec.)	Patient's time (sec.)	Activity %
1	14	31	15	14	29	18	14	31	15	14	28	18	14	31	15
2	14	28	18	14	26	19	14	31	15	14	28	18	14	31	15
3	14	28	18	15	30	18	15	30	18	15	31	17	15	31	17
4	14	26	19	14	26	19	14	31	16	14	28	18	14	26	19
5	14	34	14	14	34	14	14	35	14	14	34	14	14	34	14
6	14	32	16	15	34	16	15	31	17	15	33	16	15	31	17
7	15	25	23	15	24	25	15	25	23	15	24	25	15	25	23
8	15	25	23	15	25	23	15	24	25	15	25	23	15	26	22

clinic for examination at intervals determined by the physician-in-charge. Other visits, however, simply for the estimation of the prothrombin-time, could be obviated with advantage to both patients and staff. It is not suggested that the laboratory should take over their management by post, but that the number of visits to hospital could be reduced to a minimum. Patients living locally may continue to report at times to suit their working-hours; but, where they live far from the centre, blood could be withdrawn either by their own doctor or at a smaller hospital (where there are no laboratory facilities) and sent by post for estimation next day.

It matters little whether whole blood or plasma is sent, so long as there is no contamination with surgical spirit. Such contamination is a common cause of hæmolysis and interferes with the accuracy of the results.

It is hoped that estimations of prothrombin-time made up to 24 hours after withdrawal of the blood, without special precautions regarding storage in the interim, will reduce the very considerable labour and time expended in dealing with such patients, particularly where large numbers are involved.

It may be that the results are less accurate if there is more than 24 hours' delay, and a further study is being made to discover the effects of increasing the interval between sampling and estimation.

Summary

In the control of long-term anticoagulant therapy it makes little difference whether the samples of blood used for the estimation of the one-stage prothrombin-time are fresh or 24 hours old.

Possible therapeutic implications are discussed.

This investigation was made in the Department of Cardiology, Edinburgh Royal Infirmary. My thanks are due to Dr. A. Rae Gilchrist for his encouragement; the staff of the Clinical Laboratory, in particular Dr. Elizabeth Gilchrist, without whose coöperation the investigation would have been impossible; and Prof. I. G. W. Hill for help and advice with the paper.

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CONTROL OF HYPOTENSION FOLLOWING REMOVAL OF AORTIC CLAMPS

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THE operation of grafting segments of aorta, for aneurysm and thrombosis, carries a relatively high mortality, recorded by Rob (1955) as 17% in a series of 59 patients. The mortality is greater when the aorta is clamped at a high level—that is, immediately below or above the renal vessels; in a consecutive series of 24 patients operated upon for aneurysms or thromboses there were 8 postoperative deaths, of which 6 occurred within the first forty-eight hours; of these latter, 3 occurred on the operating-table following release of the aortic clamps, and 3 were due to coronary thrombosis occurring during the first or second postoperative day. An aortogram illustrating the type of case on which these operations were performed is shown in fig. 1.

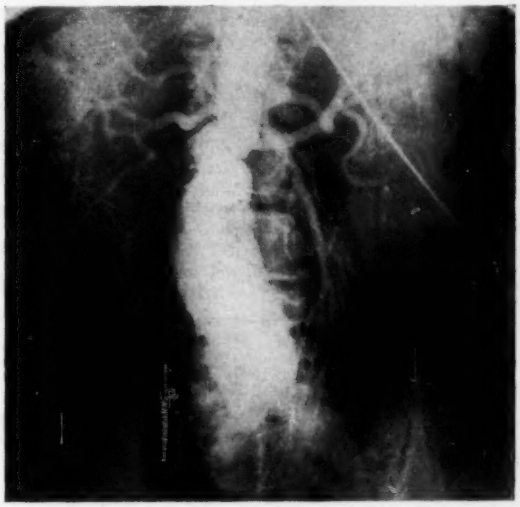

Fig. 1—Aortogram showing large aortic aneurysm.

Release of the aortic clamp results in a dramatic fall of blood-pressure, which requires a rapid transfusion of blood and frequently an infusion of noradrenaline, before a satisfactory level is restored. This period of hypotension may last for five to ten minutes, occasionally longer, and may result in a greatly diminished blood-flow through the coronary arteries and the brain, to mention two organs whose blood-flow is greatly dependent on arterial pressure. It seemed probable that the fall of blood-pressure was due to the return of blood to the previously ischæmic tissues and that it might be controlled by regulating this return. This paper records preliminary results of an attempt to achieve such control.

Calf Blood-flow

Calf blood-flows were recorded with a venous-occlusion plethysmograph in 5 of the 24 patients, during the operation and the immediate postoperative period. The plethysmograph was water-filled at 34°C, and in 2 patients operated on under hypothermia this was allowed to cool with the patient to 28°C. The volume was recorded electrically (Cooper and Kerslake 1951). Ten-second inflow traces were recorded alternating with ten-second periods of deflation of the collecting cuff. The foot circulation was isolated with a cuff round the ankle inflated to 200 mm. Hg during each three-minute period of recording. Fig. 2 is representative of the results obtained; it shows hyperæmia in the calf on removal of the aortic clamp, coinciding with the period of hypotension. The flow increases both when the patient is cooled and when he is not.

Control of Hypotension

The hypotension may be partially controlled by gradual release of the aortic clamp, but in a grafting operation there is danger of thrombosis in the prosthesis if this phase is prolonged. A simple apparatus has therefore been devised consisting of two arterial occlusion cuffs placed one on each thigh and connected to a mercury manometer and inflating mechanism, the valves being so arranged that the cuffs may be inflated or deflated independently. The cuffs are placed as high on the thigh as possible before operation and, just before the aortic clamp is released, both are inflated to a pressure greater than the systolic blood-pressure—usually to 200 mm. Hg. After release of the aortic clamp the circulation is

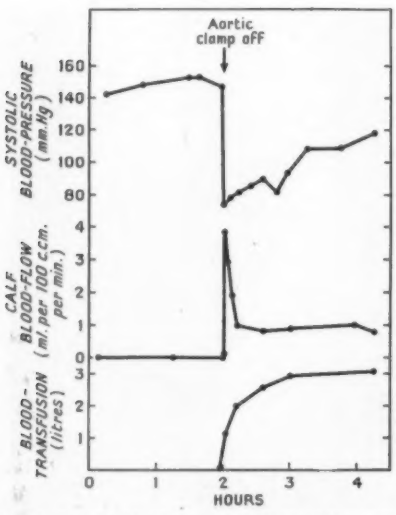

Fig. 2—Systolic blood-pressure, calf blood-flow, and blood-transfusion during resection of aortic aneurysm. Aorta clamped above the renal vessels, and bifurcation prosthesis inserted.

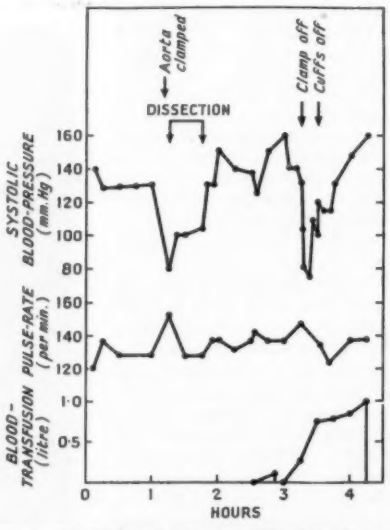

Fig. 3—Systolic blood-pressure and blood-transfusion during resection of high aortic thrombosis. Aorta clamped below renal vessels, and 'Orlon' bifurcation prosthesis inserted.

re-established in a relatively limited area of ischæmic tissue through the internal iliac, inferior epigastric, and circumflex femoral arteries, and possibly the upper profunda femoral anastomosis. When the blood-pressure has recovered from the fall so incurred, the thigh cuffs are deflated one after the other. The time for this procedure seldom exceeds twenty minutes.

This controlled re-establishment of blood-flow appears to limit the degree and duration of hypotension. Of 7 patients so managed 1 died from coronary occlusion on the third post-operative day. In addition, only 1 patient in this series has received a noradrenaline infusion during the period of hypotension.

Figs. 3 and 4 are representative charts of patients in this series and show the fall of systolic pressure resulting from release of the aortic clamp and the cuffs. It often happens that release of the second cuff only delays the rise in pressure. Fig. 4 is of particular interest because samples of blood were taken from a catheter placed in the inferior vena cava. The blood pH and the plasma-potassium level were estimated and recorded. The lowest pH determined was 6·79 and the highest K+ 8·5 m.eq. per litre, the K+ curve being a mirror image of the pH curve. This was probably due to an inadvertent rapid infusion of 3·8 litres of stored blood after an unexpected hæmorrhage. Stored blood may have a pH as low as 6·4 and a plasma-potassium level as high as 8·7 m.eq. per litre. Because of these properties of stored blood our practice is to obtain a high proportion of the total blood used in these cases fresh from the donors.

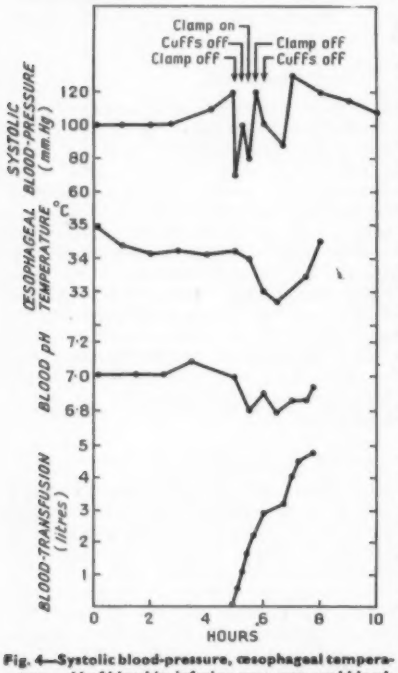

Fig. 4—Systolic blood-pressure, œsophageal temperature, pH of blood in inferior vena cava, and blood-transfusion in resection of abdominal aneurysm. Aorta clamped below renal vessels, and bifurcation prosthesis inserted.

The body-temperature was recorded with an œsophageal thermocouple placed at heart level and showed the fall of temperature resulting from re-established circulation in the ischæmic tissues and the infusion of cool blood.

Conclusion

Release of the circulation in operations for grafting segments of aorta suddenly increases the blood-flow in the legs to two or three times the resting level and considerably more than the very small flow when the aorta is occluded. There is also refilling of a partially emptied limb vascular bed. This "physiological hæmorrhage" may explain the hypotension observed, but possibly the sudden addition to the general circulation of vasodilator metabolites produced by the ischæmic tissues may contribute to it. Large infusions of whole blood and often of noradrenaline are required to compensate the fall in blood-pressure, with a resultant increase in the blood volume in the early postoperative period, thus placing an additional strain on the heart —a matter of some consequence in patients with atherosclerosis.

The use of thigh cuffs to permit a controlled release of the circulation appears to have limited the degree and duration of the hypotension in the cases reviewed. From observation of other patients in whom the aorta has been clamped at various levels for one or two hours, the cuffs appear to be of most value in the following circumstances: (1) when the aorta has been clamped proximally; (2) where a long segment of aorta is occluded; and (3) where there is little or no established collateral circulation.

Summary

Release of the aortic clamp in operations for grafting segments of the aorta causes a profound fall in blood-pressure.

A striking increase in calf blood-flow accompanies this hypotension.

A simple apparatus is described which allows a more controlled re-establishment of the circulation in such cases.

Attention is drawn to the potential danger of a rapid infusion of large quantities of stored blood.

We are very grateful to Prof. C. G. Rob for advice and encouragement; Dr. C. H. Cheetle, Dr. H. L. Thornton, and Dr. K. B. Chambers for valuable assistance, particularly in recording blood-pressure and pulse readings; and Dr. D. Sutton for permission to reproduce the aortogram.

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RESERPINE IN ANXIETY STATES

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IN psychiatry, where there is little agreement on basic theory and most forms of treatment are empirical, there tends to develop a definite pattern of response to the introduction of any new therapeutic drug. Firstly, there are the preliminary reports of clinical impressions; these will determine what range of dosage and what frequency and duration of administration are likely to be most suitable; and if (as is usually the case) the drug appears to be of value, further investigations are indicated. Secondly come the controlled trials; these may show that the effect of the new drug is no better than that of a placebo, or they may show that it possesses an efficacy which cannot be explained simply in terms of interest and enthusiasm. In this latter case comparative trials must be made of the new drug against a standard preparation and it is here that the new treatment stands or falls, for it must be shown either to possess some new therapeutic power or to be at least as efficacious as the standard treatment.

Such a pattern can be discerned in the use of reserpine, one of the alkaloids of *Rauwolfia serpentina*. First used in the treatment of hypertension, it was found to have a beneficial effect on the neurotic symptoms of hypertensive patients (Wilkins 1954). Reports followed on its use and efficacy in various mental disorders, especially in neurotic anxiety and tension. Controlled trials of reserpine in neurotic states have produced conflicting results (Davies and Shepherd 1955, Folkson and May 1955); but, even if it were established that neurotic patients improve more on reserpine than on placebo tablets, such improvement might be due simply to a non-specific sedative action of reserpine. This possibility can be tested by comparing the effect of reserpine with that of a barbiturate (*Lancet* 1955).

The aim of the present study was to make such a comparison. We used a dose of reserpine (2 mg. t.d.s.) which is rather higher than that generally used in the treatment of neurotic patients; we did this because published reports show a clear tendency towards increased dosage and a pilot study, in which patients were given this dosage for one or two weeks, did not reveal any disturbing side-effects.

Method

The value of the self-controlled and self-recorded clinical trial in low-grade morbidity has been pointed out by Hogben and Sim (1953), and the technique has been shown to give reliable results in neurotic patients (Hare 1955). Using this technique, the present investigation was planned to compare the effect of reserpine, amylobarbitone sodium, and an inert control substance on the general clinical state and certain specific symptoms in patients with neurotic anxiety.

Case-material

The patients studied were all inpatients in a neurosis unit. None was hypertensive. A patient was admitted to the trial only if his major symptoms were anxiety and tension, if he was willing and intelligent enough to coöperate, and if he appeared to be a reliable witness. 42 patients began the trial, but 9 did not complete it: 2 of these 9 discharged themselves against advice for reasons unconnected with the trial; 2 refused, during the first week, to continue, saying the tablets made them much worse (both were receiving control tablets); and in 5 cases it was considered advisable to interrupt the trial and to proceed with electroconvulsion therapy, although there was no evidence that the failure to improve or the worsening of the clinical state was associated with the administration of any particular drug.

33 patients (14 male, 19 female) completed the trial satisfactorily. In 4 of these (1 male, 3 female) the dose had to be halved after three days because of the complaint of excessive drowsiness; this happened in each case while the patient was receiving reserpine. We did not feel, however, that halving the dose seriously disturbed the course of the trial; so the records of these 4 patients have been included in the analysis of the results. The average age of the 33 patients was 42·5 years (range 23–64).

During the trial the patients received a hypnotic (mostly butobarbitone gr. 3) where this was indicated, but no other treatment was given.

Administration of Drugs

Each of the three drugs was administered to each patient for a week, the whole trial lasting three consecutive weeks. Thus the patient received two capsules and two tablets three times daily; and although the capsules and tablets remained identical in appearance they contained, for one week each, either reserpine 6 mg. daily, amylobarbitone sodium gr. 6 daily, or an inert control substance. Until the conclusion of the trial the order in which the drugs were administered was known only to the dispenser. It was arranged that, for the 33 patients, each drug was given an equal number of times in each of the three weekly periods and that (so far as was possible) each drug was preceded by each of the other two drugs on an equal number of occasions. This distribution eliminates any bias due to a tendency for the patients to feel better at the end of the trial period * and any bias due to the possibility that the effect of a drug might persist from one week to the next.

Assessment

Daily record charts were prepared on which each patient rated:

(1) How he felt compared with the previous day—"better," "same," or "worse" (scored 0, 1, and 2 respectively).

(2) The degree to which he had been affected by certain symptoms (see table I)—"absent," "mild," "moderate," or "severe" (scored 0–3).

(3) The quality of his last night's sleep—"undisturbed," "slightly disturbed," or "restless" (scored 0–2).

In addition, he completed a record at the end of each week indicating:

(1) How he had felt on the whole during that week compared with the previous week—from "much improved" to "much worse" (scored 0–4).

(2) The quality of his sleep during the week (scored 0–2).

(3) New or particularly troublesome symptoms.

Objective checks on the validity of the patients' records were made in the following ways. The charge-

* There was in fact a slight (statistically insignificant) tendency for the third week of the trial to be rated as better than the other two weeks.

TABLE I—COMBINED RATING SCORES FOR 33 ANXIETY-NEUROTICS RECEIVING DIFFERENT DRUGS (A LOW SCORE INDICATES A FAVOURABLE RESPONSE)

Symptom or sign	How often rated	Rated by	Total score for week on		
			Reserpine	Amylobarbitone sodium	Control substance
General condition	Daily	Patient	221	155	212
	,,	Nurse	231	147	189
	Weekly	Patient	60	33	58
	Bi-weekly	Physician	119	74	105
Headache ..	Daily	Patient	262	184	264
Indigestion	,,	,,	172	104	162
Palpitation	,,	,,	197	118	192
Sweating ..	,,	,,	121	78	129
Trembling	,,	,,	372	171	243
Dizziness ..	,,	,,	276	196	213
Drowsiness	,,	,,	360	293	272
Depression	,,	,,	352	269	336
Anxiety and tension	,,	,,	365	267	343
	Bi-weekly	Physician	180	142	165
Other somatic signs	Bi-weekly	,,	84	52	65
Sleep ..	Weekly	Patient	29	27	38
	Daily	,,	208	166	238
	,,	Nurse	722	714	829

nurse of the ward kept an independent daily record in which he assessed each patient's daily condition as "improved," "same," or "worse" (scored 0–2). The night-nurse kept a sleep-chart recording the number of half-hourly periods between 10 P.M. and 6.30 A.M. that the patient was observed to be awake (scored 1 for each half-hour awake). The physician in charge of the case recorded twice weekly :

(1) His assessment of the patient's general clinical condition compared with the previous period—from "much improved" to "much worse" (scored 0–4).

(2) The presence of anxiety, tension and other somatic signs—"absent," "slight," "moderate," or "severe" (scored 0–3).

(3) The patient's blood-pressure, measured under standard conditions.

Finally, at the conclusion of each patient's trial but before he knew the order in which the drugs had been given, the physician rated each weekly period as better, equal to, or worse than each of the other two weekly periods.

Results

Table I shows the totals of the scores obtained from 33 patients. Since a low score means a good clinical response, it is clear that on the whole the patients felt better, both generally and for particular symptoms, when receiving amylobarbitone sodium than when receiving either reserpine or the control substance. It is also clear that there is little or no difference between the response to reserpine and that to the control substance.

Table II compares the weekly periods on the different drugs, assessed by the physician at the completion of the trial. Evidently there is nothing to choose between the effects of reserpine and of the control substance. The periods on amylobarbitone sodium, however, are for the most part better than either those on reserpine or those on the control substance ; the expected proportion of "better" periods on amylobarbitone sodium (on the null hypothesis) lies in each case outside the 99% confidence limits of the observed proportion.

TABLE II—NUMBER OF TIMES THE GENERAL CLINICAL CONDITION OF THE PATIENTS RECEIVING THE FIRST-NAMED DRUG WAS BETTER, EQUAL TO, OR WORSE THAN THEIR CONDITION WHEN RECEIVING THE SECOND-NAMED DRUG

Drugs	Comparative clinical response		
	Better	Equal	Worse
Reserpine *v.* control substance	15	3	15
Amylobarbitone sodium *v.* control substance	27	1	5
Amylobarbitone sodium *v.* reserpine ..	25	1	7

Comparison of the blood-pressure readings for different weeks of the trial gave (for 29 patients only) the following mean values :

	Reserpine	*Amylobarbitone sodium*	*Control substance*
Systolic pressure (mm. Hg) ..	127·5	130·2	137·5
Diastolic pressure (mm. Hg)	72·3	76·2	79·2

The systolic pressures were lower during the reserpine week than during the control week in 24 of the 29 patients ; and the diastolic pressures were lower in 21 of them. These figures suggest that reserpine was exerting a definite, if slight, hypotensive effect.

The principal side-effects—i.e., new or troublesome symptoms—noticed by the patients are shown below, together with the number who mentioned them while receiving the different drugs :

Symptom	*Reserpine*	*Amylobarbitone sodium*	*Control substance*
Drowsiness	11	7	3
Dizziness	8	6	4
Nasal congestion	6	—	—
Swelling of ankles	2	1	1
Increased appetite	2	—	1
Dyspepsia	2	1	1
Headache	1	—	—
Nightmares	2	1	2

Objectively there were no obvious signs attributable to the drugs ; no parkinsonian rigidity was observed. The occurrence of side-effects in patients receiving inert control substances is, of course, well recognised (Wolf and Pinsky 1954).

Discussion

The effects of drug treatment in an anxiety state are possibly best assessed by the self-observation, under controlled conditions, of a coöperative and intelligent patient making a comparative rather than an absolute assessment of the intensity of his symptoms. Bias due to casual environmental factors or to apparently spontaneous fluctuations in the degree of anxiety can, to a great extent, be eliminated by using a blind self-controlled technique and a reasonably large series of cases. A further advantage of the self-controlled and self-recorded clinical trial is that it enables the reliability of the patients' records to be checked. We may summarise the evidence which tends to confirm the reliability of the patients' records in the present trial as follows :

(1) The patient's scores on different drugs are closely paralleled both by those of the charge-nurses and those of the physicians.

(2) The sleep assessments are mutually consistent.

(3) The only instance in which a score on amylobarbitone sodium exceeds that on the control substance is for the patients' daily rating of "drowsiness," and this corresponds to expectation. Again, although for the most part there is little difference between the scores on reserpine and those on the control substance, the reserpine scores for "drowsiness," "dizziness," and "trembling"—all recognised side-effects of reserpine treatment—are much higher.

As regards the duration for which the drugs were exhibited in the present trial, it might be objected that a week is not long enough for reserpine to exert an adequate effect. However, there is ample evidence that the reserpine was exerting its action in producing side-effects, as well as its probable effect in lowering blood-pressure (the hypotensive effect of reserpine in normotensive people has been demonstrated by Freis and Ari [1954]). It seems unlikely that the effect of a drug on anxiety could be delayed for more than a week when its other effects are manifest within a day or two. Moreover, amylobarbitone sodium, which also caused side-effects within a day or two, could clearly influence the mental state within the same short period.

A more cogent criticism of the present findings is that any possible benefit from reserpine was offset by the unpleasant side-effects associated with the rather high dosage used. That these side-effects could be trouble-

some is shown by the fact that in 4 cases the dose had to be halved. However, only one of the reserpine side-effects (drowsiness) was really troublesome to the patients, and (as shown above) drowsiness often affected the patients receiving amylobarbitone sodium (also in rather high dosage). Yet, with amylobarbitone sodium, drowsiness did not stop the patients from recording that they felt improved. This was not so with reserpine and at least 3 patients on reserpine specifically recorded that although they felt more drowsy and physically relaxed than before the trial began they felt no less anxious. A similar "dissociated" response in a psychotic patient has been described by Tyndel (1955).

It is worth noting that the patients in this trial were almost entirely new cases, many of them being recently admitted to hospital for the first time. They therefore received the benefit of full initial examination and assessment on admission, together with general reassurance. There was no suggestion that their treatment was experimental, the patients simply being told that they were to receive a special three-week course of tablets and capsules. The conditions of the trial were such that the findings are not invalidated by any improvement due to suggestion, since the conditions were the same during the administration of each of the drugs and the experimental method was based on a comparison between different periods and not on an absolute assessment. In such circumstances, especially when the periods are relatively short, this type of trial acts as a combined treatment and research project, and it is very doubtful whether (in the interests of attaining scientific objectivity) the refinement of telling the patient that this is a new treatment, and that the physician does not know whether or not it will be helpful, is necessary or even advisable.

The general conclusions to be drawn from this trial are that, for a week and in the dosages given, amylobarbitone sodium caused much improvement in the general condition and in the individual symptoms of the great majority of patients with anxiety neurosis, whereas the effect of reserpine was no better than that of an inert control substance. This does not mean, of course, that in smaller doses or administered for longer periods, reserpine could not be beneficial in anxiety states, but it suggests the need for caution in accepting some of the enthusiastic reports of the efficacy of this drug; and it also suggests that, at least on a short-term basis, amylobarbitone sodium is of definite value.

Summary

A comparison was made of the effects of reserpine 2 mg. t.d.s., amylobarbitone sodium gr. 2 t.d.s., and an inert control substance on 33 patients with neurotic anxiety. Each drug was administered for a week.

A self-controlled self-recorded technique was used. The reliability of the records was checked by internal evidence and by objective assessment.

Compared with the control week, most patients recorded much alleviation of their anxiety symptoms when they received amylobarbitone sodium, but there was no general tendency to alleviation when they received reserpine.

We wish to thank Mr. E. F. Wellington and Mrs. J. Silcock, pharmacists, for their assistance, and the nurses for their coöperation with the record charts. Ciba Laboratories Ltd. kindly supplied the reserpine ('Serpasil') and the matched control tablets, and Eli Lilly Ltd. the amylobarbitone sodium ('Sodium amytal') and matched control capsules.

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ACUTE AND LATENT PORPHYRIA

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DURING the past five years we have encountered 8 cases of acute porphyria and discovered 4 cases of latent or symptomless porphyria in one family. Since the area served by our hospitals is not a large one (population 150,000) we considered that acute porphyria is commoner than is generally realised. We report the results of our study of the inheritance of the disorder, and discuss the factors that may precipitate an attack of acute porphyria.

The clinical and biochemical classification of the porphyrias is controversial, but in this report the terms acute and latent porphyria are used to describe patients excreting excessive amounts of porphobilinogen in the urine without sensitivity of the skin.

Material

The investigation is based on 6 women and 2 men whose ages ranged from 20 to 59 years (see accompanying table). Cases 4 and 6 are first cousins and case 8 is the mother of case 9. We have traced the family history of every patient and interviewed many relatives. Specimens of urine were obtained from absent relatives and their medical history learned by correspondence with them and their practitioners.

Examination of Urine

Colour

The urine of patients with acute porphyria, even during acute episodes, may be a normal colour, or it may be orange and dismissed as "concentrated." If the urine is left in daylight for a few hours, there is a definite alteration in colour, the urine becoming amber, particularly near the surface where it is in contact with air. This simple test may be used as a preliminary test in a patient's home or at a cottage hospital where there are no laboratory facilities. Urines from patients who have had blood-transfusions may also darken on standing, owing to the presence of other pigments; and therefore inspection of urine, even after allowing it to stand for some hours, is of limited value in the diagnosis of acute porphyria.

In the laboratory, the darkening of the urine in cases of porphyria may be enhanced by heating it in a water-bath for ten minutes and then comparing the colour with that of an unheated control.

Biochemical Tests for Porphobilinogen and Porphyrins

The urine excreted by all patients with acute porphyria (whether in the active or the latent phase of the disease) contains porphobilinogen. This is the biochemical criterion necessary for diagnosis.

Porphobilinogen is a colourless chromogen, but it can be identified by a simple chemical test using Ehrlich's aldehyde reagent, our technique being a slight modification of that proposed by Watson and Schwartz (1941).

To 2 ml. of urine add 2 ml. of Ehrlich's aldehyde reagent (0·7 g. of *p*-dimethylaminobenzaldehyde in 250 ml. of 6 *N* hydrochloric acid). Mix and allow to stand for two minutes and then compare the colour with a mixture of 2 ml. of urine and 2 ml. of 6 *N* hydrochloric acid (this is a safeguard against artefacts caused by foodstuff colours excreted in the urine). Porphobilinogen gives a red colour which develops within twenty seconds, and urobilinogen gives a similar colour. If a red colour is obtained, allow the mixture to stand for two to three minutes and then add 4 ml. of chloroform and shake the test-tube; if the red colour remains in the aqueous layer the colour is due to porphobilinogen, but if it passes to the chloroform layer it is due to urobilinogen. Normal urines give no red colour.

CASES OF ACUTE PORPHYRIA

Case	Sex	Age (yr.)	Medication	Neurological complications	Outcome
4 (1st attack) .. (2nd ,,) ..	M	20	0·5 g. thiopentone for laparotomy Gr. 3 quinalbarbitone	None Paralysis of both arms ten days later	Recovered Recovered
6 (1st attack) .. (2nd ,,) .. (3rd ,,) ..	F	21	Thiopentone for appendicectomy Thiopentone for laparotomy, and gr. 1½ butobarbitone daily for six days afterwards Gr. 20 barbitone sodium and gr. 4 phenobarbitone for several days in a mental hospital	None None Complete paralysis of both arms and legs	Recovered Recovered Died
8 (several attacks)	F	59	Large doses of various barbiturates at mental hospitals	None	Died (from carcinoma of stomach)
9	F	36	Gr. 1 phenobarbitone and gr. 3 quinalbarbitone daily for four days	Paralysis of arms fourteen days later	Recovered
10	F	55	Gr. 1 phenobarbitone and gr. 3 quinalbarbitone daily for seven days	Paralysis of both arms and legs	Died
11	F	21	0·5 g. thiopentone for laparotomy followed by gr. 2 phenobarbitone for fourteen days	Paralysis of both arms and legs seventeen days after laparotomy	Died, 8 weeks pregnant
12	M	58	Gr. 2 phenobarbitone daily for a month before attack	None	Recovered
13	F	44	0·5 g. thiopentone for laparotomy; gr. ½ phenobarbitone and gr. 1½ butobarbitone for six days after operation	None	Recovered

If it is not possible to carry out the test shortly after the urine has been passed, it should be stored in the dark and tested within twenty-four hours.

In addition to porphobilinogen, the urine of patients with latent or acute porphyria may contain porphyrins, which can be detected by the 2 following techniques.

Ultraviolet fluorescence.—A filtered urine, preferably after standing overnight, is examined under ultraviolet light with a Wood's glass filter. A distinctive red to salmon-pink fluorescence indicates the presence of porphyrins. To show the fluorescence more clearly, the porphyrins may be concentrated in an amyl-alcohol extract of urine acidified with a few drops of acetic acid.

Spectroscopic examination with the dark-vision spectroscope shows two bands at 577 and 541 mμ. These are due to a porphyrin-metal complex and are very similar to the bands of oxyhæmoglobin; but if the urine is made strongly acid by adding 25% *v/v* of concentrated hydrochloric acid, a porphyrin spectrum may be seen at 597 and 553 mμ. It is advisable to test various depths of urine, because a poor spectrum may be obtained with too much or too little urine.

Further differentiation of the porphyrins into the various isomers and quantitative determination has proved of little value in the diagnosis of acute porphyria.

During the past two years, all urines sent to the laboratory have been tested for porphobilinogen and we have been rewarded by finding 2 cases of acute porphyria: case 12 was being treated at home by his practitioner for abdominal pain, and case 13 was in a surgical ward recovering from a cholecystectomy which had failed to relieve her pain.

Hammond and Welcker (1948) carried out a similar investigation of the urines of 1000 patients with various diseases, but failed to find any cases of porphyria. Nevertheless, the Watson-Schwartz test is simple to perform; and a mass survey of a population group would provide information concerning the prevalence of latent porphyria, which is at present unknown.

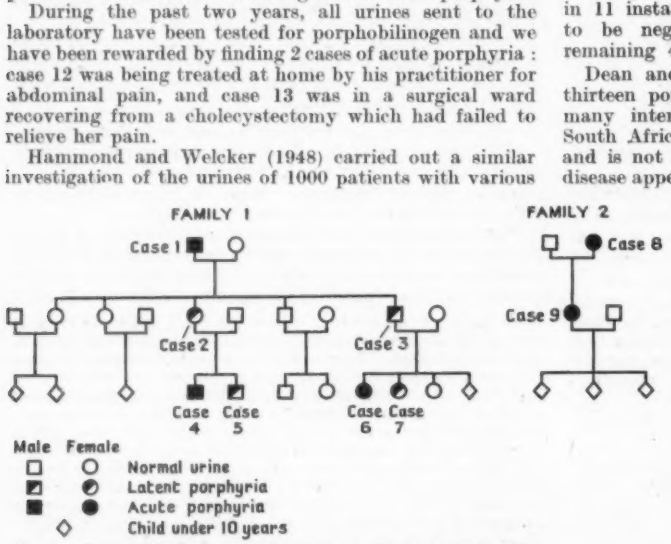

Fig. 1—Acute and latent porphyria in two families.

Inheritance

Günther (1912) recognised that porphyria was an inborn error of metabolism, and Waldenström (1937) was able to follow the transmission of acute porphyria in nine families through two, and in one family three generations. He considered that the families might be descended from a common ancestor and that the defect was inherited as a dominant character not linked to either sex. Gates (1946) studied Waldenström's families and other evidence of inheritance in acute porphyria, and concluded that the dominance is often irregular, and that possibly two factors are involved.

Although there have been many reports of cases of acute porphyria in England, especially in the past few years, the family history is frequently stated as negative, and we have been unable to trace any family tree in which dominance could be demonstrated. Markovitz (1954) reviewed all case-reports published in the English language between 1941 and 1953. These numbered 69, and a proven or suspected family history was reported in 11 instances; in 17 the family history was stated to be negative, and it is not mentioned in the remaining 41.

Dean and Barnes (1955) studied the genealogies of thirteen porphyric families, all of Burgher stock with many intermarriages, and showed that porphyria in South Africa is inherited as a mendelian characteristic and is not sex-linked. In these families, however, the disease appeared in the acute form, the chronic cutaneous form (the "cutanea tarda" type), or a symptomless porphyrinuria; and in many cases one clinical type changed into the other. These workers regard acute porphyria and porphyria cutanea tarda as different manifestations of the same inherited disorder but in this country Calvert and Rimington (1953) showed that it is possible to distinguish them, for in porphyria cutanea tarda during remission the fæcal porphyrin level is raised.

In the present study we have found more than 1 case of acute porphyria in each of two families (fig. 1). Dominance was demonstrated in family 1; but in four other affected families we have been unable to trace any inheritance of the defect.

Case-reports

FAMILY I

CASE 1.—The grandfather of cases 4 and 6. This man died in 1940 at the age of 64, and unfortunately we lack proof that he had acute porphyria. Nevertheless, we have questioned his widow and his doctor, and think that the attacks of abdominal pain from which he suffered during the later years of his life (and for which no cause was found) were symptoms of acute porphyria. In addition, the records of his last illness describe extensive paralysis, which his widow asserts was very similar to that of her grand-daughter. Members of his family state that his urine was sometimes very dark, but, as far as we can trace, it was never tested for porphyrins.

CASE 4.—A man, aged 20, and a first cousin of case 6. While he was serving in the R.A.F. his urine was found to contain moderate amounts of porphobilinogen. He was in good health and had not had abdominal pain or other symptoms suggesting acute porphyria. We therefore classified him as a case of latent porphyria and warned him of some of the inherent dangers of the disease. A few weeks later, and shortly after the death of his cousin, he had a severe attack of abdominal pain associated with constipation and was admitted to a hospital in another part of the country as a case of suspected appendicitis. He informed the surgeon that he had porphyria, and the presence of porphobilinogen in his urine was confirmed; but laparotomy was performed under thiopentone anæsthesia and a healthy looking appendix was removed. He made an uneventful recovery from the operation, but was discharged from the R.A.F. on medical grounds. Three months later he had a further attack of severe abdominal pain. We had asked his practitioner not to give him any barbiturate drug; but he was attended on this occasion by a locum practitioner, who prescribed gr. 3 of quinalbarbitone ('Seconal'). On his admission to hospital the next day an increased amount of porphobilinogen was found in his urine, and his systolic and diastolic blood-pressures were raised 20 mm. Hg above the usual levels. The attack of abdominal pain subsided in a few days, but ten days after the onset he complained of weakness of both arms and fairly extensive paralysis of the muscles of both shoulders and arms developed. He made a slow but good recovery during the next few months. During the past two years, this patient has had four further bouts of abdominal pain, but barbiturate drugs have not been prescribed and there have been no neurological complications. Porphobilinogen has been found in his urine whenever it has been tested; and the amount is greatly increased during an attack of abdominal pain.

CASE 6.—A married woman, aged 21, was admitted to hospital with complete paralysis of all limbs and some weakness of the intercostal muscles (fig. 2). Her urine was a port-wine colour and the diagnosis of acute porphyria was confirmed by finding that the urine contained large quantities of porphobilinogen and porphyrins. During the previous three years the patient had had several attacks of abdominal pain for which two laparotomies were performed; on the first occasion a healthy looking appendix was removed, and on the second some adhesions were divided. The attacks of abdominal pain continued and she underwent a course of psychiatric treatment, including sedation with large doses of barbiturate drugs, after which weakness in both legs developed and she became completely paralysed in all limbs. Despite many forms of treatment the patient died five months after admission to hospital.

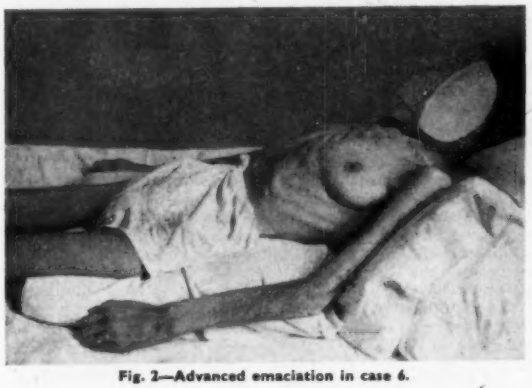

Fig. 2—Advanced emaciation in case 6.

Latent Cases

CASE 2.—The father of case 4, aged 45. He has no symptoms of acute porphyria; but his urine is often pink and contains a moderate amount of porphobilinogen.

CASE 3.—The mother of case 6, aged 43. She has no symptoms of acute porphyria; her urine is a normal colour but contains porphobilinogen.

CASE 5.—The brother of case 4, aged 19. He has no symptoms of acute porphyria; his urine is a normal colour but contains porphobilinogen.

CASE 7.—The sister of case 6, aged 20. She has no symptoms of acute porphyria. This patient has had two confinements without complications. Her urine is normal in colour but contains porphobilinogen.

FAMILY II

CASE 8.—The mother of case 9. She was treated for "plumbism" at the age of 35, and had a severe attack of abdominal pain for which a laparotomy was advised when she was 40. She refused operation and the pain subsided in a few days; she was free of attacks between the ages of 40 and 59 when they recurred several times a year. Despite numerous investigations, including radiography, no cause to account for the pain was found and she received psychiatric treatment, including electroconvulsive therapy, in mental hospitals. After her daughter had had an attack of acute porphyria, her urine was examined and found to contain much porphobilinogen. She died at the age of 64 from carcinoma of the stomach.

CASE 9.—A married woman, aged 36, was admitted to a surgical ward with lower abdominal pain and constipation. She was treated with enemas and given gr. $^1/_2$ phenobarbitone twice daily and gr. 3 quinalbarbitone at night; the abdominal pain was relieved in a few days and she was discharged from hospital. She was readmitted to a medical ward fourteen days later with weakness of both arms; her urine was dark and contained porphobilinogen. During the next few days, paralysis of the extensor muscles of both wrists developed, and tests confirmed weakness of several other muscles in both arms and forearms. With active physiotherapy she eventually made a complete recovery, but she has continued to pass varying amounts of porphobilinogen in the urine for the past four years. During this time she has had occasional attacks of abdominal pain and has twice been admitted to hospital for observation. No barbiturate drugs have been given and there have been no further paralytic episodes. She became pregnant last year and gave birth to a healthy girl; her urine contained moderate amounts of porphobilinogen during the confinement.

OTHER CASES

Our 4 other patients with acute porphyria (cases 10–13) came from different families; but although we investigated many relatives, including the parents of cases 10 and 12, we found among them no cases of latent porphyria.

CONCLUSIONS

The inheritance of the defect in acute porphyria as a dominant was confirmed in family 1. In view of the negative family histories in many well-authenticated cases, we think it possible that more than one factor is involved, or that affected members of the family excrete porphobilinogen intermittently or in such small amounts that it cannot be detected by the Watson-Schwartz test.

Precipitation and Features of Acute Attacks

Watson (1954) states that the mechanism by which the latent disease becomes manifest is unknown, and he suggests that there are various precipitating factors.

Günther (1912) referred to "toxic" porphyria because of the frequency with which acute attacks followed the ingestion of sulphonal and 'Trional.'

Waldenström (1937) administered a barbiturate to a woman who had never had an acute attack but whose sister had had

acute porphyria. After ingesting the drug she had an attack for the first time.

The sulphonamide group of drugs and alcohol have also been incriminated, but the evidence against these substances is less strong than in the case of the barbiturates.

The borderline between remission and relapse in acute porphyria appears to be very easily shifted, although too little is known of the factors responsible for the change in either direction.

During the present study, case 9 had five attacks of acute porphyria in four years and case 4 had four attacks in two years. Both patients were coöperative and intelligent, and we were able to obtain a most detailed history of the onset of the attacks, special attention being paid to any unusual physical or mental stress or any dietetic abnormalities during the fortnight preceding the attack. In each case, and in each attack, the clinical manifestations were similar :

The patient was in good health, carrying out the normal duties of a housewife or a factory worker. The first symptom was colicky pain in the lower abdomen, which increased in intensity and often became continuous and lasted for several days. The patient became constipated, but this did not precede the onset of abdominal pain by more than one day, or at most two. The patients noticed that their urine became darker than usual and they became extremely apprehensive ; both patients had neurological complications during previous attacks.

On examination the patient's temperature was slightly raised but not above 100°F. The pulse-rate was increased by about 20 beats per minute, and both systolic and diastolic blood-pressures were raised by about 20 mm. Hg. There was tenderness on superficial and deep palpation of the abdomen but no rigidity or rebound tenderness. Nevertheless, these signs may easily be confused with those caused by an inflamed appendix lying in the retrocæcal position, and case 4 was operated upon at another hospital although the surgeon knew that he had porphyria.

Investigations.—The urine was either dark when passed or became so on standing, and contained porphobilinogen and porphyrins. The serum-bilirubin level was sometimes slightly raised (1·5–3·0 mg. per 100 ml.), but other liver-function tests gave normal results ; and the rise in the serum-bilirubin level remains unexplained. The attacks passed off in a few days and the patients recovered rapidly. Both of them have become more pigmented during the past two years, and hirsuties has developed in case 9.

We are unable to suggest any precipitating cause for the recurrent attacks of acute porphyria in these 2 patients. They had received no drugs, and there was no history of physical or mental stress, or of minor infections before the attacks. No unusual food or drink had been taken and there was no excessive sexual indulgence. No treatment was given, and we are equally ignorant of the factors which caused the attacks to subside.

Rôle of Barbiturates in Acute Porphyria

In the past few years Rimington and his colleagues have made great advances in our understanding of the rôle of barbiturates in porphyrin metabolism (Goldberg and Rimington 1955).

Goldberg (1954) showed that various barbiturate hypnotics, especially those containing allyl groups, induced porphyric changes in the rabbit. He also pointed out that barbiturates can inhibit some of the oxidative processes of brain tissue (Quastel and Wheatley 1933). Goldberg suggested that in addition to the possibility of a direct effect of a barbiturate drug on porphyrin metabolism, the hypnotic activity may aggravate the upset in brain and nerve metabolism described in acute porphyria by Denny-Brown and Sciarra (1945).

Many reports emphasise the deterioration in the condition of patients with acute porphyria after the administration of barbiturate drugs (Prunty 1946, Jørgensen and With 1947). On the other hand, Turner (1938) and Discombe and D'Silva (1945) failed to note any relation between barbiturates and acute porphyria.

All our patients were given barbiturates during one or more attacks of acute porphyria, and the complications that followed are recorded in the table. It will be seen that the effect of giving barbiturate drugs during an attack of acute porphyria is unpredictable.

Cases 8, 12, and 13 received barbiturates but recovered from attacks without any complications. In case 4 paralysis of both arms developed after administration of gr. 3 of quinalbarbitone, although in a previous attack the patient had received 0·5 g. of thiopentone for a laparotomy and made an uneventful recovery. Case 6 had three attacks of acute porphyria, during each of which she received barbiturates. There were no complications on the first two occasions, but on the third very large doses of barbitone sodium and phenobarbitone were given at a mental hospital and she became completely paralysed in all limbs. On the other hand, case 8 had received similar treatment, also in a mental hospital, and she did not have any paralysis.

These data are insufficient to provide any conclusions as to the harmful effects of slow-acting, as distinct from long-acting, barbiturates ; or concerning those containing an allyl group, which according to Goldberg (1954) produced the greatest rise of porphyrin in rabbits' urine.

In addition to our own cases, we studied many reports of other patients suffering from acute porphyria with neurological complications, and we were struck by the fact that all the patients had received some form of barbiturate medication—although in some cases paralysis of muscles was not noted until ten days after the barbiturate had been given (e.g., case 4). Because cases of latent porphyria can have acute abdominal symptoms without having received any barbiturate drug (as in the later attacks in case 4 and in case 9), we suggest that the rôle of barbiturates in acute porphyria may be related more to neurological complications than to the precipitation of an acute attack.

Pregnancy

Waldenström (1937) reported that 2 of his patients had died from acute porphyria during pregnancy, and he suggested that the hypnotic and other drugs given during this time might have been responsible. He also thought that pregnancy itself might have precipitated an attack of acute porphyria, and Watson (1952) said that this might happen after a confinement. On the other hand, Freedman et al. (1952) reported that a patient with acute porphyria had improved during and after pregnancy.

One of our patients was pregnant when acute porphyria was first diagnosed (case 11) and 2 others became pregnant during the course of the investigation (cases 9 and 7).

CASE 11.—A married woman, aged 21, was admitted to a surgical ward with a history of abdominal pain, vomiting, and constipation for five days. She had had a normal period three weeks previously, and the surgeon who examined her thought that she had a twisted ovarian cyst. A laparotomy was performed under thiopentone anæsthesia, but no abnormality was found ; a recently ruptured ovarian follicle was seen. The abdominal pain persisted and she was treated with gr. 2 of phenobarbitone daily. On the day after operation the ward-sister noticed that she was passing dark urine ; but the significance of this was not appreciated, and it was not until she became paralysed in both legs on the twelfth day after operation that her urine was found to contain large quantities of porphobilinogen. She died from respiratory paralysis a week later ; an early fœtus was found in the uterus at necropsy

This patient had had no previous attacks of abdominal pain, nor any symptoms suggesting acute porphyria. The urine of 6 of her relatives was tested for porphobilinogen, but none was found. She had received no drugs before the onset of the pain, and we concluded that conception had played some part in the precipitation of the attack of acute porphyria.

CASE 9.—This patient had had two attacks of acute porphyria (with paralysis of her arms on the second occasion) when she told us that she was very anxious to have a third

child. In consultation with Prof. C. H. Gray we strongly advised her against such a course, but nevertheless she became pregnant a year later and was safely delivered of a baby girl with the aid of pethidine. During pregnancy, she had two mild attacks of abdominal pain and passed moderate amounts of porphobilinogen in her urine, but the amount was not increased at delivery or during the puerperium.

CASE 7.—This patient, aged 20, is a case of latent porphyria belonging to family 1. She has had two normal confinements without an acute attack of porphyria developing, and she hopes to have more children. Apart from avoiding barbiturate drugs, no special precautions were taken during her pregnancies. The amount of porphobilinogen passed in the urine was not increased during her last confinement.

Comments

The factors which cause a patient with latent porphyria to have an acute attack are unknown, but many instances between the ages of 18 and 30 (when pregnancy is most likely) have been reported. Possibly the bad reputation which pregnancy has acquired as a precipitating cause of acute porphyria is in part due to the coincidence of the period of greatest fertility with the age-group which is most susceptible to acute porphyria.

Mental Symptoms

It is well known that mental disturbance is a common accompaniment of acute porphyria, and Markovitz (1954) reported that mental changes were noted in over three-quarters of the 69 patients in his review. In the present study, cases 6, 8, and 12 had spent periods in mental hospitals, and cases 4, 9, and 11 had psychological upsets during porphyric attacks. Cases 6 and 11 died, but the other patients recovered and their mental state became normal as the attack subsided. In addition, we observed no mental disturbances in 4 cases of latent porphyria (family 1), and we suggest that the so-called porphyric temperament is not a common feature of the disease. The histories of many patients with acute porphyria is a lamentable tale of wrong diagnoses, unnecessary operations, and sedation or shock treatment; possibly these vicissitudes may have caused the "nervous constitution" mentioned in some reports. This should not be confused with the mental symptoms that often accompany attacks of acute porphyria.

Treatment

The efficacy of any treatment is notoriously difficult to assess in acute porphyria, in which spontaneous remission and rapid improvement are common (Rimington and Goldberg 1954). During the past five years, we have treated ten attacks of acute porphyria in 7 patients with one or more of the following drugs: neostigmine, potassium and calcium salts, corticotrophin, cortisone, 'Eucortone,' and large doses of vitamin B_{12} and other vitamins. No beneficial effect was noted, and rational therapy must await a clearer understanding of the chemical pathology of the disease.

On two occasions acute attacks were accompanied by a striking decrease in the serum-sodium level (to 103 m.eq. per litre in case 12, and 118 m.eq. per litre in case 13). Both patients were considerably improved by infusions of normal saline, and we agree with Davies (1949) that careful control of the electrolyte balance is essential during acute attacks.

When abdominal pain is severe or during a confinement we use pethidine; and paraldehyde is preferable to barbiturate drugs as a sedative for patients with mental symptoms; although the pathogenesis of porphyria is at present unknown, barbiturate drugs should not be prescribed. We treated 3 patients in artificial respirators, but they all died.

Cases 4 and 9 survived an attack during which the muscles in the shoulders and arms were paralysed, and we were agreeably surprised by the full recovery of function that they achieved with physiotherapy—and in a shorter time than is usual for a similar paralysis caused by poliomyelitis.

Summary

In five years 8 cases of acute porphyria have been found in a population of 150,000.

Inheritance by mendelian dominance has been demonstrated in one family.

The precipitation of an acute attack and the influence of barbiturates and pregnancy are discussed.

Mental disturbance is a common accompaniment of acute porphyria.

We thank Prof. C. Rimington, F.R.S., and Dr. A. Goldberg for their help and interest in this investigation, and Dr. A. I. Cheyne for allowing us to study case 10.

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DIARRHŒA DUE TO PHENOLPHTHALEIN

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THE exact diagnosis of many cases of chronic diarrhœa often remains in doubt; they may be labelled "colitis," nervous or lienteric diarrhœa, and so on. Further elucidation of this ill-defined group will depend on more complete and accurate methods of investigation. Routine use of fat-balance tests to assess the function of the small intestine has, for example, already shown that idiopathic steatorrhœa is the cause of many such cases (Cooke et al. 1953). The technique for the fat-analysis of the stools that we now use is essentially that of van de Kamer et al. (1949), by which the total fatty acids excreted are estimated daily. The two following cases of diarrhœa due to phenolphthalein were discovered accidentally by this method. Such a cause was quite unsuspected, and the diagnosis would otherwise have been missed.

Case-reports

Case 1.—A man, aged 30, complained of attacks of intermittent diarrhœa for nine years. He said they had begun in 1943, when he started to pass frequent bloodstained stools after being captured in Germany while serving as a commando. His weight fell during imprisonment from 12 st. to 7 st. in six months. Although the diarrhœa improved it continued until his release in 1945. After treatment in a British hospital it gradually improved until 1951. Between October, 1950, and November, 1951, he had ten attacks of abdominal pain and vomiting with diarrhœa. Investigation in another hospital in November, 1951, included sigmoidoscopy, which showed ulcers suggesting old amœbiasis. No amœbæ were seen, nor

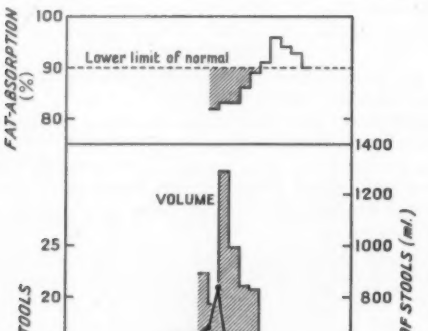

Fig. 1—Fat-absorption and number and volume of stools (three-day means) of case 1 on a diet containing 50 g. of fat daily: *hatched area*, period in which phenolphthalein was detected in fæces.

were any dysenteric organisms isolated. A full course of anti-amœbic treatment was given, the diagnosis being ulcerative colitis following amœbic dysentery. Attacks of diarrhœa continued after his discharge from hospital; and, during an attack while he was visiting Birmingham, he was admitted to the Queen Elizabeth Hospital under the care of Prof. T. L. Hardy.

On examination there was no obvious wasting, and no abnormal physical signs were detected in the alimentary system. Rectal examination was normal. Sigmoidoscopy showed slight reddening of the mucosa, but the appearance was considered to be within normal limits, and no granularity or ulceration was noted up to a distance of 15 cm. The patient appeared very concerned about his condition, gave a long and detailed account of his illness, and was obviously introspective.

Laboratory Investigations.—His stools were brown and semi-formed or fluid, and microscopy showed them to contain an excess of fatty-acid crystals but no pus or blood. A barium meal ('Raybar') was normal, and a barium enema showed no ulcerative colitis or other colonic lesion. A glucose-tolerance test and chylomicrograph showed somewhat low rises in blood-sugar level and chylomicron counts respectively but were within the normal ranges. A blood-count was normal. During a fat-balance test on a controlled daily intake of 50 g. of fat the patient had an acute attack of profuse watery diarrhœa similar to those he had had in the past. In the most acute phase twenty stools a day were passed, associated with an excessive fæcal volume. Fat-absorption during the early part of the attack was defective. Details of the number of stools, fæcal volume, and fat-absorption are shown in fig. 1. At the height of the diarrhœa it was noticed that the addition of alkali to a fæcal aliquot turned it pink, and spectrophotometry of an alkaline filtered aqueous fæcal extract showed the absorption spectrum of phenolphthalein. The disappearance of the pink colour on the addition of concentrated sodium hydroxide confirmed the identification as phenolphthalein. When phenolphthalein had been found in the stool on four or five consecutive days, the patient was asked if he were taking laxatives. This he denied, and a search of his possessions revealed none. Within two days of this questioning, however, the attack of diarrhœa ended abruptly, an alkaline extract of his fæces was no longer pink, and his fat-absorption became normal.

Psychological investigation subsequently showed an intelligent patient, with great emotional tension and a background of incompatibility in marriage. Moreover the question of attributability of his disability to Army service had been raised on several occasions. In spite of this psychological background, the attack of diarrhœa observed in hospital was considered to be caused by the patient's taking phenolphthalein.

Case 2.—A married woman, aged 41, complained of attacks of diarrhœa and fæcal incontinence ever since anterior and posterior colporrhaphy had been done nine months earlier for stress incontinence of urine. Two attacks had developed during convalescence and further attacks later with increasing frequency, and diarrhœa had been almost constantly present before her admission to hospital. She passed up to eight loose stools in the day-time and often two at night, and she had been incontinent both by day and by night. Her stools were very watery and contained mucus but no blood. She appeared to give a good factual account of her disability and was regarded as a good and coöperative witness. She said she was inclined to worry about small things in her home life; she had had some "spells of dizziness and sickness," but there seemed nothing abnormal in her previous history to explain her condition. She had seen a doctor only once during the nine months in which the diarrhœa appeared to have been a constant feature of her daily life.

On examination no abnormality was detected apart from some pallor.

Investigations.—Sigmoidoscopy showed normal mucosa up to a distance of 25 cm. A barium meal showed mild flocculation of the barium in the small intestine in the two-hour and three-hour films, and the cæcum was small and spastic. Stomach, duodenum, and terminal ileum were normal. A barium enema showed a normal colonic outline, but the colon was irritable, and the patient evacuated its contents on to the X-ray table. A blood-count showed a mild hypochromic normocytic anæmia, which subsequently responded to iron therapy. Stools passed in hospital were loose and brown and were passed once or twice daily except on the first two days, when she passed five daily. The fæcal fat was measured daily, with the patient on ordinary ward diet, by a modification of the method of van de Kamer et al. (1949). The amount of fat excreted was within normal limits. During the process of estimation it was noted that the alkaline fæcal emulsion was pink on ten days. The urine passed in twenty-four hours was collected on five days, and on only one of these days did the addition

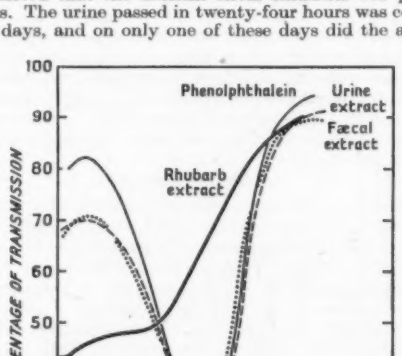

Fig. 2—Absorption curves relevant to case 2.

of alkali turn it pink. The pigment was extracted from the fæces and urine and identified as phenolphthalein (see below). After phenolphthalein had been seen in the stool for about seven days, the patient was asked if she had been taking laxatives. At first she denied taking any, but subsequently she admitted that she had taken two doses of a laxative since admission to hospital. After questioning, her diarrhœa ceased, her stools became formed, and phenolphthalein disappeared from her stools.

Extraction and Identification of Pigment

The pigment was identified in aqueous alkaline solution spectrophotometrically. In case 2 it was extracted from

fæces and urine first with amyl alcohol and then redissolved in aqueous sodium hydroxide. Phenolphthalein 65 mg. given to another person was readily identified in the stool by the same procedure. The extraction of rhubarb with amyl alcohol yielded solutions which became red when redissolved in sodium hydroxide, owing to chrysophanol (also present in senna), but the colour was different to the eye from that of phenolphthalein and its absorption-curve was different (fig. 2).

Discussion

Though both patients denied taking laxatives at the material times, diarrhœa ceased abruptly after they had been questioned about this. The disappearance of diarrhœa coincided with the disappearance of phenolphthalein from the stools. There seemed therefore to be good reason to believe that the diarrhœa was due to the phenolphthalein, and that their word could not be accepted. Although in both patients there was some psychopathic background, malingering could not be ruled out.

Most of the average dose (60–240 mg.) of phenolphthalein is excreted in the fæces because phenolphthalein is rather insoluble (von Vamossy 1902), and some of the absorbed portion is excreted in the bile. Phenolphthalein excreted in the urine is in the free form (after large doses only) and conjugated as sulphate and glycuronate, mainly the former, in which state it does not turn pink on the addition of alkali unless it is first liberated by hydrolysis by boiling with hydrochloric acid. It may be excreted for several days in the conjugated form after a single dose (Fantus and Dyniewicz 1937). A simple confirmatory test would therefore seem to be examination of the urine for free and conjugated phenolphthalein.

In the present cases diarrhœa was possibly initiated by either a single large dose or several smaller doses, but the urinary investigations were too few to indicate the dosage.

It is difficult to estimate how often this type of case occurs, but in a review of 1000 consecutive gastro-intestinal cases Soper (1938) found 177 habitual takers of purgatives containing phenolphthalein; 152 of these cases had been diagnosed as catarrhal colitis. Soper noted that symptoms of colitis disappeared when the offending drug was withdrawn, but he did not state in how many this sequence of events was seen. Ease of detection must vary with the purgative used. In the present cases detection was made simple by the readiness with which phenolphthalein appeared when the fat-balance was being estimated by the method of van de Kamer et al. (1949).

The steatorrhœa seems worth recording. Phenolphthalein effects purgation primarily by preventing the absorption of water from the large or the small intestine or both; it does this directly by stimulating the motor mechanism and indirectly by increasing the intestinal secretion and thus the bulk of the contents, to which the intestine responds by increased peristalsis (Fleig 1908, Ott and Scott 1908, Blick et al. 1942). The presence of excess fat in the stool indicates that the small intestine is involved in the process. The fat-absorption defect may thus be the result of an acute diarrhœa due to small-intestine hurry.

Summary

Two cases of diarrhœa due to self-medication with phenolphthalein are described and the methods of detection outlined.

Attention is drawn to the possible importance of self-induced diarrhœa as a clinical syndrome and a further cause of steatorrhœa.

We wish to thank Prof. T. L. Hardy and Dr. C. F. Hawkins for permission to publish cases 1 and 2 respectively; Dr. H. G. Sammons and Mr. John Taylor for help with the analyses in case 1; and the United Birmingham Hospitals Endowment Research Fund, the Mackenzie Mackinnon Trust, and the Medical Research Council for financial assistance.

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Preliminary Communication

TREATMENT OF HYPOPHOSPHATASIA WITH CORTISONE

We have previously reported[1] certain metabolic abnormalities in a female infant with hypophosphatasia.

The patient presented at the age of 5 months with markedly defective skeletal calcification, particularly in the metaphyseal regions. The total-serum-calcium level was elevated, the inorganic phosphorus was normal, and the alkaline-phosphatase activity was considerably below normal. The patient has been under our observation for the past sixteen months, and until seven months ago the skeletal lesions were becoming more pronounced, though slow linear growth of the long bones was taking place.

In June, 1955, we were led to postulate that a disturbance in adrenal cortical function was producing the skeletal lesions in this child. In consequence we administered cortisone to suppress adrenal function. The administration of 100 mg., and later 50 mg., of cortisone for a total period of two months did not alter the radiographic picture and produced toxic side-effects. However, a reduction in the serum-calcium level and an elevation of the serum-alkaline-phosphatase activity to low normal values encouraged us to administer a somewhat lower dose of cortisone. Within three weeks on 37·5 mg. of oral cortisone daily, radiographic evidence of mineralisation appeared in the long bones at the zones of provisional calcification, and within the next seven weeks very considerable calcification took place in the metaphyseal, diaphyseal, and subperiosteal regions. The bones were continuing to grow and their appearance was approaching normal. During this second period of cortisone therapy the total-serum-calcium and alkaline-phosphatase levels again became normal.

Schlesinger et al.[2] have shown that spontaneous and sometimes rapid improvement can occur in hypophosphatasia, and for this reason we have withdrawn cortisone on three occasions. In each instance the alkaline-phosphatase activity fell to pre-treatment levels within two weeks. Moreover, during a two-month period without therapy we have observed a recurrence of defective calcification in the new matrix which was laid down at the growing ends of the long bones.

From these findings we believe that cortisone produced a remission of many or all of the pathological features in our case of hypophosphatasia. At present we do not know whether the beneficial effects of cortisone were mediated indirectly through suppression of abnormally functioning adrenal tissue or whether they were due to a direct pharmacological action on the disease process.

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Medical Societies

ASSOCIATION OF CLINICAL PATHOLOGISTS

THE 56th general meeting of the association was held at Cheltenham on April 5–7. There follow brief reports of some of the papers read at the meeting.

The Rose-Waaler Test

Dr. C. L. GREENBURY, Dr. A. G. S. HILL, Dr. R. SPALDING SMITH, and Dr. M. S. GOOD had had over two years' experience with a modification of the Rose-Waaler test in a series of 700 patients, including 249 with rheumatoid arthritis. The test was positive in 90% of all cases of rheumatoid arthritis, and in 93·5% of those with positive X-ray findings. A few cases of rheumatoid arthritis were negative early in the disease, but for the most part even the earliest cases gave good positive results. There was no relation between activity, judged either clinically, by erythrocyte-sedimentation rate, or by C-reactive protein, and a positive test.

Most of the tests were done in duplicate, using saline and 2·5% sheep serum as diluents for the test sera. When sheep serum was used as diluent, titres were 2–16 times higher than with saline, and a few sera were positive in serum but negative in saline. Sera producing agglutination of sensitised cells in a dilution of 1 : 16 or higher were taken to be positive, providing that heterophile antibody was present in minimal quantity or had previously been absorbed.

It was found, in common with other workers, that serum in "collagen disease" also gave positive results. Two further groups of patients were found to give positive results: an at present ill-defined group of patients attending skin clinics; and patients with diffuse pulmonary fibrosis, finger clubbing, and arthralgia, but no arthritis. It was concluded that the Rose-Waaler test, at least in the modification described, was a most useful and accurate aid to diagnosis.

Tubeless Gastric Analysis

Dr. JOHN HARKNESS recalled that Segal et al.[1] had recommended an azure-A/cation-exchange-resin compound in which the quininium of the present tubeless gastric analysis is replaced by a dye which eventually colours the urine. This new compound still had the disadvantages of interference by drugs and food, and by the need for an injection of histamine to verify achlorhydria. Dr. Harkness proposed that a more reliable test was to estimate the overnight urinary excretion of quinine after an oral dose of 500 mg. of quinine carbonate suspended in weak alcohol or water. Food and drugs did not affect the result. Although histamine was not given, it was claimed that this technique could detect the false achlorhydrias missed by the standard intubation alcohol-histamine fractional test-meal. A satisfactory test could be carried out by a patient in his own home. Achlorhydrics excreted 0–100 μg. quinine in eight hours (further experience might increase the upper limit slightly); patients with free hydrochloric acid in the gastric juice excreted 320–30,000 μg. in eight hours.

Platelet 5-hydroxytryptamine in Blood Disorders

Dr. R. M. HARDISTY and Dr. R. S. STACEY had conducted an investigation to determine whether the incidence of purpuric manifestations in various blood disorders was related either to the concentration of 5-hydroxytryptamine (5-H.T.) in the platelets or to the total 5-H.T. content of whole blood. The platelet 5-H.T. concentration was estimated, and whole-blood 5-H.T. determined, in 83 patients with various disorders of the blood and reticulo-endothelial system, including leukæmias, polycythæmia vera, lymphomas, pernicious anæmia, and simple iron-deficiency anæmia, and in 15 non-hæmatological patients.[2] Low mean platelet 5-H.T. concentrations were found in a high proportion of cases of all the hæmatological disorders, and these often resulted in low whole-blood 5-H.T. Experiments on the absorption of 5-H.T. by platelets in vitro suggested that these low platelet 5-H.T. concentrations were attributable to a defect of the platelets themselves. The mean platelet 5-H.T. concentration in these cases was unrelated both to the blood-platelet count and to the incidence of abnormal bleeding. All but 2 of the patients with purpuric manifestations had both thrombocytopenia and a whole-blood 5-H.T. below normal limits, but the incidence of bleeding was less critically related to the whole-blood 5-H.T. than to the platelet count. Dr. Hardisty and Dr. Stacey concluded that the bleeding of thrombocytopenia cannot be attributed solely to 5-H.T. deficiency, and that there are no grounds for supposing that a low platelet or whole-blood 5-H.T. concentration, in the absence of thrombocytopenia, may be a cause of abnormal bleeding.

1. Segal, H. L., Miller, L. L., Plumb, E. J. *Gastroenterology*, 1955, **28**, 402.
2. Hardisty, R. M., Stacey, R. S. *J. Physiol.* 1955, **130**, 711.

Streptococci in a Maternity Unit

Dr. J. D. ALLAN GRAY described the spread of group-A hæmolytic streptococci among the staff and patients of a maternity unit. It began among the pupil midwives with a succession of sore throats which did not yield to sulphonamides, penicillin, holidays, or tonsillectomy. In spite of strenuous efforts, the organism spread among 55 of the staff and 57 of the patients. The vast majority of both staff and patients showed either no evidence of infection or at most only a trivial illness. 2 infants died: 1 was thought to have had a cerebral injury and the other developed his fatal illness after his discharge from hospital. While a combination of penicillin and streptomycin was required to eliminate the streptococci from the staff, penicillin alone was sufficient to eliminate them from the patients. The striking difference between the staff and the patients in the difficulty with which the streptococci could be eradicated was eventually shown to be due to the presence of penicillinase-producing staphylococci in the noses of most of the staff.

Sudden Death in Infants

Dr. J. L. EMERY and Dr. E. M. CRAWLEY had found that in a series of 50 sudden unexpected deaths in infants the history as obtained by the coroner was consistent in only 5 cases with histories obtained after the child had been buried. The histories obtained by the coroner's officer were substantially inconsistent with both morbid anatomical findings and later histories in 33 cases. The follow-up histories indicated some abnormality in all infants before death, and, in the majority, symptoms of over two days' duration. The inadequate histories might be due to the shock of the tragedy to the mother, and to the fear produced by the police and the coroner's investigations. The procedures connected with these "sudden deaths in infancy" apparently needed revision.

Salivary Tumours

Dr. J. M. CAMERON and Dr. A. DICK had studied 88 cases of salivary tumours with particular attention to the pleomorphic adenomata or the so-called mixed tumours. The parotid gland was the most frequent site, followed by the submandibular and sublingual glands in that order. They first occurred between the third and fifth decades but no age was exempt, and their growth was extremely slow. The tumour recurred in about 30%, whatever the treatment. Dr. Cameron and Dr. Dick supported the view that the cartilage-like material in many of these tumours was in fact not true cartilage but a myxo-chondroid substance developed by degeneration from epithelium and stroma.

Acute Renal Failure after Head Injury and Operation

Dr. W. H. TAYLOR and Dr. J. V. O. REID defined acute renal failure as a blood-urea level greater than 100 mg. per 100 ml. and a urinary urea level of less than 2·0 g. per 100 ml. Such failure developed after surgical operation or head injury in 25 patients who were examined post mortem. In 15 there was histological evidence of acute tubular necrosis. In 3 of the earliest cases, casts were seen to be produced by hæmorrhages from capillaries into tubules. These hæmorrhages might be important in the process of cast formation. Of the 10 patients without acute tubular necrosis, 1 had normal kidneys and 9 showed only hydropic changes in the tubules. In at least 4 of these cases the duration of acute renal failure exceeded forty-eight hours, and this should have been long enough for acute tubular necrosis to have become manifest.

Previously described clinical features of acute renal failure were not consistently present in either the tubular necrotic or non-necrotic groups. All 11 patients had oliguria (less than 300 ml. of urine per day). The plasma/urine chloride ratio was greater than 4/1 in all patients except 3 with acute tubular

necrosis, so that unregulated tubular loss of chloride with a plasma/urine ratio of about 2/1 was not a characteristic feature. The specific gravity of the urine was fixed between 1008 and 1014 in only about a quarter of the cases.

Dr. Taylor and Dr. Reid concluded that after head injury and operation acute renal uræmic failure may be present in the absence of histological tubular necrosis, and that when there is tubular necrosis its characteristic clinical features may be absent, thus causing confusion in diagnosis.

The "Buffy Coat" in Anæmia in Pregnancy

Dr. H. B. GOODALL described how microscopic examination of the "buffy coat" from the hæmatocrit had been applied to the investigation of anæmia in pregnancy. By giving a remarkably true reflection of the type of erythropoiesis in the marrow, it had enabled the diagnosis of "pernicious anæmia of pregnancy" to be made even when the rest of the peripheral-blood picture was not characteristic. During this investigation it was also found that erythrophagocytosis is not uncommon in the blood of pregnant, parturient, and puerperal patients. The possibility that the ingested red cells were fœtal had in one case been confirmed by differential agglutination, but in other instances the phenomenon might merely indicate a hæmolytic process affecting the maternal erythrocytes.

Pituitary Necrosis in Raised Intracranial Pressure

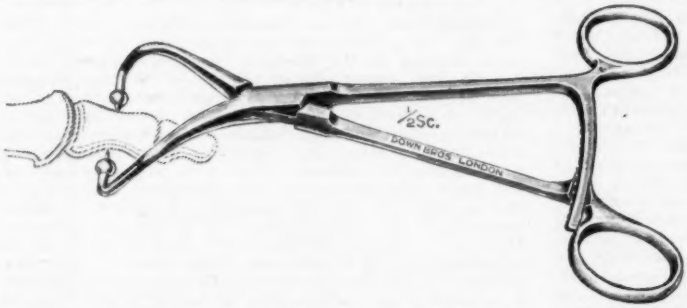
Dr. LIONEL WOLMAN said that among 270 patients dying with a tentorial pressure cone resulting from a unilateral space-occupying lesion, 12 instances of recent necrosis of the anterior lobe of the pituitary were found. The necrosis due to infarct ranged in extent from a small solitary area to as many as five discrete areas occupying most of the pars glandularis, but separated from each other and from the capsule by a zone of intact tissue. The age of the infarcts, histologically assessed, could be correlated with the probable duration of tentorial coning. The blood-supply to the anterior lobe passing down the hypophyseal stalk was considered to be impaired by the distortion of the optic chiasma, hypothalamus, and infundibulum. The mechanism which produced these infarcts seemed to be quite distinct, and Dr. Wolman separated this group from postpartum necrosis of the pituitary and from various other causes.

New Inventions

HALLUX FORCEPS

THE forceps here portrayed are designed to hold the proximal end of the 1st phalanx in Keller's operation for hallux valgus. (The diagram shows the forceps holding the bone in the centre rather than more proximally.)

These forceps are strong and they grip the base of the bone firmly, and slight rotation can be carried out. The base of the bone can, therefore, be dissected more easily away from the flexor tendon. They are also useful in other procedures such as patellectomies, and in the operative treatment of certain fractures.



The instrument is made by Messrs. Down Bros. and Mayer & Phelps, and I am indebted to Mr. V. G. Carter of that firm for his help in their design and construction.

W. E. TUCKER
C.V.O., F.R.C.S.

London

Reviews of Books

Outline of Orthopædics

JOHN CRAWFORD ADAMS, M.D., F.R.C.S., consultant orthopædic surgeon, St. Mary's Hospital, London. Edinburgh: E. & S. Livingstone. 1956. Pp. 423. 32*s*. 6*d*.

THIS is a book for students, and a very welcome one. It aims to give "an easily read account of our present knowledge and thought on orthopædic surgery in the shortest possible compass consistent with accuracy, and without resorting to the style of a synopsis." Orthopædics is now so vast a subject that the success of such a book depends as much on the author's choice of what to leave out as of what to put in; and on the whole Mr. Adams has done admirably.

Nearly a third of the book is a general survey of orthopædic disorders; this is necessarily superficial, but it probably covers the irreducible minimum which the student must know. The later chapters on specific regions contain very useful and orderly sections on history-taking and physical examination; and throughout the book there is constant and admirable emphasis on the clinical side. Some may wish to see more stress laid on the need always to have the other limb exposed for comparison. The diagrams are clear and most of the radiographs are outstandingly good.

The individual surgeon may find many points open to criticism, and he might reasonably say that some of the text, particularly that dealing with the ætiology of certain conditions, is rather old-fashioned—but perhaps this is good for the examinee. If the student cannot feel with his hands that one trochanter is higher than the other, will the construction of Bryant's triangle really help him to decide the point? Some will be disappointed that there is so little indication of where manipulative methods of treatment may be helpful.

On the whole, however, Mr. Adams succeeds splendidly in his difficult task, and his book should be in steady demand by medical students.

Pharmacopœia Internationalis

Geneva: World Health Organisation. 1955. Vol. II. Pp. 350. 35*s*. Also published in French.

THE first volume of the first edition of the *International Pharmacopœia* was published three years ago, and it is gratifying to learn from the preface to volume II that its predecessor was given a good reception and is now in wide use. The origins and scope of volume II are stated succinctly by the editorial committee:

"The urgent need for the publication of volume I, which arose from the developing activities of the World Health Organization in co-ordinating and unifying the health activities of its Member States, led to the omission from that volume of certain drugs concerning which rapid advances in knowledge and practice were being made. Volume II supplies these omissions and deals with various forms of insulin, with tubocurarine chloride, and with the antibiotics chloramphenicol, chlortetracycline, dihydrostreptomycin, oxytetracycline, penicillin and streptomycin. Some synthetic chemical drugs of recent introduction to therapeutics are included and an attempt is made to complete the information given in volume I by including, in appropriate instances, monographs on compressed tablets, sterile injections, and tinctures."

The scope of the work is now comparable to that of the older national pharmacopœias. Here and there, however, there are signs of compromise—which is perhaps as well in a work that symbolises international coöperation. This attitude presumably explains the inclusion of a number of drugs and preparations which are in eclipse in English-speaking countries. When, in 1955, monographs are published on bismuth subnitrate, bismuth salicylate, amidopyrine, aconite, sodium barbitone, and tincture of digitalis, some people may wonder whether national fashions have got the better of good judgment. The

International Pharmacopœia, however, is in its infancy: in the years ahead its virility will be revealed in its lists of additions and deletions.

The bulk of the text is devoted to the 217 monographs. Appendices, which form a supplement to those included in volume I, occupy about a third of the book. They range over conventional chemical methods, biological assay, and tables of constants. There is a schedule of "usual and maximal doses for most drugs," and another showing "usual daily doses for children." These are useful but they do not compensate for the omission of doses from the monographs. The dosage tables also suffer because they are incomplete. The *International Pharmacopœia* breaks new ground by its inclusion of a section on solutions of cardiolipin and lethicin for serological tests. This "annex" was printed at the request of the subcommittee on serology and laboratory aspects of the Expert Committee on Venereal Infections and Treponematoses. It creates a precedent of considerable importance to compilers of pharmacopœias.

Neural Control of the Pituitary Gland

G. W. HARRIS, SC.D., M.D., F.R.S., Fitzmary professor of physiology, Institute of Psychiatry, Maudsley Hospital, London: London: Edward Arnold. 1955. Pp. 298. 30*s*.

IN this readable monograph Professor Harris describes the functioning of both the anterior and the posterior lobes of the pituitary gland. As might be expected, his own work figures prominently in his account, and he admits in his preface to some bias in the presentation of material. But he has produced a fascinating story which is sufficiently consistent to be readily followed and remembered yet does not belittle the uncertainties which still exist.

The book begins with an account of the anatomy of the hypothalmus and hypophysis with special reference to their blood-supply, and this is followed by a discussion of the mechanisms controlling secretion of the gonadotrophins, adrenocorticotrophin, and thyrotrophin. In later chapters it reviews briefly but adequately the regulation of the anti-diuretic factor and gives a clear and useful account of the hormonal aspects of parturition and lactation. Neuro-secretion receives brief but favourable mention, and the last chapter considers the hormonal influences which affect behaviour patterns in primates and other mammals.

Professor Harris not only deals admirably with his special subject, but also touches informatively on many topics of general endocrinological interest.

Diabetes

G. F. WALKER, M.D., M.R.C.P. Pp. 96. 8*s*. 6*d*.

Cancer and Allied Diseases

RONALD W. RAVEN, O.B.E., T.D., F.R.C.S. Pp. 121. 8*s*. 6*d*.

Childbirth

W. C. W. NIXON, F.R.C.S., F.R.C.O.G. Pp. 106. 8*s*. 6*d*.

London: Duckworth. 1955.

THESE are three more volumes in the Modern Treatment series, intended for the general public. Though not written for that purpose, they throw much light on current medical thought and practice. They show an increasing desire to enlighten patients about normal and abnormal bodily happenings, about the medical approach to them, and about the modern medical armament—preventive and curative. This rapport between doctors and patients is most desirable; but it is no easy thing to achieve. To translate technical language (often, some would say, jargon) into lucid, unambiguous English is hard enough; to ensure that the translation will convey the true meaning to the lay reader is harder still; and to warn and advise without sowing fears or adding to the difficulties of the reader's own doctor is perhaps hardest of all. The authors of these small books sometimes succeed in this difficult task but sometimes, perhaps inevitably, they fall short in one way or another.

Diabetes contains much excellent practical advice, but the explanatory sections may not leave the reader much clearer about the nature of the disorder. Unlike the other two, this book has no glossary or index.

Cancer describes the nature of normal and malignant cell-multiplication and deals with radium, radiotherapy, and chemotherapy in some detail. With the glossary's aid, the reader should be able to grasp what he is told. In the clinical section, cancers of certain organs and regions have been chosen for relatively detailed description, including those of the pharynx, the liver, and the blood (leukæmia)—but not (rather surprisingly) tumours of the larynx, thyroid, prostate, or bladder, which usually have more specific early symptoms and are more amenable to treatment. The discerning reader will find the book grim reading: the absence of reliable warnings and the inefficacy of treatment for many sorts of malignant disease is all too clear. Would it not have been better to concentrate on those few which an intelligent patient really can "catch in time" if he has the knowledge?

Childbirth has an admirable account of labour from the "labourer's" point of view, with effective photographs of models showing the nature of the birth process. A chapter of "Any Questions?" includes a clear and comforting exposition of the rhesus situation. Diet looms large in pregnancy: food two-hourly, no fried food, no salt at table, strict weight-control, and no liquid paraffin. With visits to clinics, systematic relaxing practice, and perhaps exercises, even the primigravida must have a busy time; and one imagines that the mother of one or two with a husband who fancies fried bacon would find the burden heavy.

Sexual Precocity

HUGH JOLLY, M.D., M.R.C.P., consultant pædiatrician, Plymouth Clinical Area. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1955. Pp. 276. 50*s*.

SOME years ago Dr. Jolly started to study sexual precocity; hitherto those who wanted to know his conclusions have had to refer to an admirable but meagre paper in the *Proceedings of the Royal Society of Medicine*—that is, if they had not had the opportunity to read the thesis which won him the Raymond Horton Smith prize. Now they can consult the full monograph, nicely produced in the United States and correspondingly priced.

More than half the book is taken up by case-reports, many of them illustrated. Sexual precocity in the physical sense, bewildering when first encountered, is seen to be resolvable into four groups: constitutional (in which the child is normal in every other way, perhaps merely exemplifying how widely normal variation may extend), intracranial (hypothalamic-pituitary), gonadal, and adrenal. In the first two there is premature puberty (which implies the production of ova or spermatozoa); in the others there is not. To these may be added the cases produced by the administration (intentional or accidental) of stilbœstrol. More of them may be seen now that potent endocrine preparations are so widely used.

Until Dr. Jolly's book is superseded by one written on the basis of investigations and theories yet unimagined, anyone thinking about a difficult case of sexual precocity can confidently turn to it for guidance.

Poliomyelitis (2nd ed. London: Edward Arnold. 1956. Pp. 147. 16*s*.).—After four important years, full of developments bearing on the treatment and prevention of poliomyelitis, the second edition of Dr. W. Ritchie Russell's book will be widely welcomed as an up-to-date survey. Some controversial matters, such as the value of exercising paretic muscles to the point of fatigue during the convalescent (rehabilitation) stage, are now better explained, especially in the light of the author's further work on muscle recovery. Too timid physiotherapy is still condemned, and a timely plea is made for the wider adoption of methods of actual measurement of muscle strength, as by the spring-balance. This aspect of the subject, like many others, is well illustrated by photographs, line drawings, fatigue records, and other graphs. Changes in the treatment of the acute stage, especially in respiratory and bulbar cases, are similarly well surveyed. The method of intermittent positive-pressure respiration, introduced by the Danish school, now falls into its natural place, not as a first choice, but for patients for whom the tank respirator is inadequate. Pathogenesis is dealt with in a graphic and satisfying way, particularly the changes in the motor nerve-cells. It would be hard to find anywhere an account of the clinical aspects of poliomyelitis so concise and yet so comprehensive.

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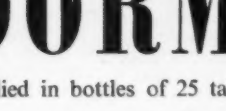

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THE LANCET

LONDON: SATURDAY, APRIL 28, 1956

Fats and Disease

SINCE the time of THUDICUM,[1] chemists have been systematically engaged in elucidating the complex structures of the lipids found in biological materials. Present knowledge of the subject is summarised in simple language in a small monograph by LOVERN,[2] and set out more fully in the new edition of HILDITCH's authoritative treatise [3]; and these clearly show that the variety of the lipids and the specificity of their chemical constitution is second only to that of the proteins. Physiologists have been slow to unravel the biological significance of these differences in chemical structure, and only in the past few years have attempts been made to assess their importance in pathology, and especially to appreciate the possible rôle of different fats in the ætiology of degenerative diseases. Three weeks ago SINCLAIR [4] indulged in some fascinating speculations arising from the view that the sophisticated diets of modern urban man are relatively deficient in the fatty acids, linoleic and arachidonic. These acids contain 2 and 4 double bonds, and BURR and BURR [5] showed many years ago that they were essential in the diet of rats if growth was to be maintained and dermatitis prevented. Most nutritionists have held that human diets are never significantly deficient in these acids, but SINCLAIR thinks that relative deficiencies, associated with a high intake of saturated fatty acids and a low intake of vitamin B_6, may predispose to a variety of degenerative disorders including atheroma and myocardial infarction. In their article this week Dr. BRONTE-STEWART and his colleagues in Cape Town provide evidence, from trials on man, that the nature of the dietary fat affects the lipid content of the serum: oils in which a high proportion of the fatty acids are unsaturated—i.e., most vegetable oils and those derived from fish and marine mammals—consistently depress serum-cholesterol levels.

As ANFINSEN [6] points out, lipids are transported in the plasma and through the extracellular fluids in three forms:

1. As chylomicra, which are large particles, usually visible under the microscope. They are mostly composed of triglycerides, but their detailed chemical architecture remains a mystery.
2. As β-lipoproteins, which contain about 25% of protein per particle and include varying proportions of cholesterol, triglyceride, and phospholipid.
3. As α-lipoproteins, which contain relatively more protein and less lipid and so have a higher density.

It is now established that patients who have had a recent infarction of the myocardium have a high level of β-lipoproteins in their plasma and this is associated with high levels of cholesterol.[7] The fact that atheromatous plaques contain large quantities of cholesterol adds circumstantial evidence that the infarction and the disorder of fat transport in the blood are causally related. Moreover, studies of the blood-clotting mechanisms have shown that some of these may be intimately connected with fat transport. KORN [8 9] has demonstrated that the clearing of fat from the blood after a fatty meal is brought about by a lipoprotein lipase, which is a tissue enzyme. The enzyme is present in heart muscle and in adipose tissue, and its high degree of specificity of action on the triglycerides of lipoproteins and chylomicra apparently depends on the presence of heparin: indeed, heparin may possibly be a component prosthetic group of this enzyme. ROBINSON and POOLE [10] have been studying the effect of chylomicra, present in the blood after a fatty meal, in making the blood more coagulable, and adduce evidence that this effect is specifically due to the presence in the chylomicra of ethanolamine phosphatide—a substance which resembles lecithin in chemical composition except that the choline base is replaced by ethanolamine. Normally, ethanolamine phosphatide probably constitutes only 5–10% of the total phospholipid in chylomicra; and studies of the factors which may increase this percentage may well provide a clue to chemical processes responsible for pathological thrombosis. The specific chemical properties of lipids are now beginning to be related to pathological processes.

The great importance of the work of BRONTE-STEWART and his colleagues lies in the assumption that any dietary factor that raises or lowers the level of β-lipoproteins in the blood will also, by implication, raise or lower the liability to myocardial infarction. In their experiments on volunteers it was shown that ingestion of beef dripping, butter, hydrogenated ground-nut oil, and eggs in large numbers was followed by rises in β-lipoprotein levels in the plasma: on the other hand, ingestion of olive oil, ground-nut oil, sunflower-seed oil, arachis oil, seal oil, or pilchard oil was associated with falls in, or low levels of, serum-β-lipoproteins. Food fats and oils thus seem to fall into two classes, whose effects on plasma-lipids are antagonistic to each other. If these results are substantiated, coronary-artery disease becomes in part a preventable disorder—but at the cost of a complete revolution in our present-day dietary habits. The hydrogenation plants of our modern food industry may turn out to have contributed to the causation of a major disease. To preserve the unsaturated fatty acids in vegetable oils and marine oils, and to make these oils palatable and acceptable to industrial populations would be a herculean task for those who would seek to change people's eating habits. All the principles of the modern margarine industry might have to be put into reverse. However, comments on Dr. SINCLAIR's hypothesis from Professor YUDKIN in our last issue and from Prof. ANCEL KEYS this week indicate that systematic knowledge of the ratio of essential to total fatty acids is far from complete for single artificial dietary fats, and it is almost non-existent for the total fats consumed in the diets of any large group of persons. Thus more knowledge of actual fatty acids in the diets of populations is needed

1. Thudicum, J. L. W. Reports of the Medical Officer of the Privy Council and Local Government Board. 1874. New series, **3**, 113.
2. Lovern, J. A. The Chemistry of Lipids of Biochemical Significance. London, 1955.
3. Hilditch, T. P. Chemical Constitution of Natural Fats. 3rd edition. London: Chapman & Hall. 1956. Pp. 664. *95s.*
4. Sinclair, H. M. *Lancet*, April 7, 1956, p. 381.
5. Burr, C. O., Burr, M. M. *J. biol. Chem.* 1929, **82**, 587.
6. Anfinsen, C. B. Arteriosclerosis. Symposium of the Minnesota Heart Association and the University of Minnesota. *Min. Med.* 1955. **38**, 767.
7. See *Lancet*, 1955, ii, 1123.
8. Korn, E. D. *J. biol. Chem.* 1955, **215**, 1.
9. Korn, E. D. *Ibid*, p. 15.
10. Robinson, D. S., Poole, J. F. C. *Quart. J. exp. Physiol.* 1956, **41**, 36.

before it will be possible to decide how variations in that ratio affect the prevalence of disease.

SINCLAIR also postulates that the use of flour of low extraction-rate would significantly lower the effective content of the national diet in essential fatty acids and so predispose to atheroma and myocardial thrombosis and increase the prevalence of other diseases of civilisation, which he suggests may be attributable to relative deficiencies of these acids. Here he is on very uncertain ground and can muster no direct experimental support. He is right, however, in urging the need for more research on these problems; and in the present state of our ignorance it is surely rash to commit most of our population to consuming bread made from a flour about whose nutritive properties we know so little and have so many genuine doubts.

Research into the origins of degenerative diseases of man is beset with difficulties. Laboratory animals can be of only limited help, since in general they are much less susceptible than man. It is also clear that noxious processes must persist for a long period before overt disease is manifest. In this type of research the unit of time is the decade. For the most part physiologists are still preoccupied by what happens in a few milliseconds, and even experimental pathologists like to get their results in a few weeks. Established methods of medical research are thus not well suited to tackle the problems of the degenerative diseases. The Cape Town workers are to be congratulated on the ingenuity with which they have devised an experiment which has established an important differential in the physiological effects of various dietary fats and oils. They have, however, demonstrated effects lasting for only a few days: clearly we should like to know that the vegetable and marine oils not only lower lipoprotein levels but can keep them low for long periods. Their present findings, however, will be a stimulus to others to follow their clear lead in elucidating one of the gravest medical problems of industrial communities.

A Merger?

HOSPITALS are very important and very impressive; but they ought not to dominate the medical scene, as they do now. Whether people remain well and happy depends mainly on what happens to them, and is done for them, outside hospital; and we have repeatedly expressed our opinion that more of the resources of the National Health Service should be going into the kind of preventive and curative medicine that cannot be practised properly except where people live and work. This view was put forcibly by Prof. FRASER BROCKINGTON on Tuesday at the Blackpool meeting of the Royal Society for the Promotion of Health.[1]

Last century, he said, all doctors in this country recognised that health is very largely a matter of environment; and as long ago as the 1830s disease was studied as a community problem. But a hundred years later, in the 1930s, it had become customary to think of illness chiefly as a hospital episode. Already the profession had retreated from its position of leadership in the challenge to environment, and "from the most enlightened of public-health pioneers, we have become the most backward, giving pride of place to the underdeveloped regions of the world. To see public health in action, one must now go to Yugoslavia, Africa, Thailand, or to other and unmentionable places." One reason for this, paradoxically, is that public health has been so successful here, in eliminating the more obvious and dramatic plagues, that some people imagine it has nothing left to do; another may be that the appointment of medical officers of health has made the rest of the profession feel that public health is no longer their concern; but the principal single reason is the growth of interest in institutional care—which the National Health Service, so far from diminishing, has accentuated. Under the N.H.S. the hospitals are better organised, better staffed, and (taking it all in all) more efficiently and economically run than before; but BROCKINGTON holds that, in terms of public health, their nationalisation has been little short of disastrous; for they have been unnaturally elevated to a position of pre-eminence, and are absorbing the best of the brains, and the lion's share of time and effort and money. "The environment, upon whose inadequacies the whole of the apparatus of medicine is in reality constructed, has slowly receded into the background of our thoughts."

The primary need now, as BROCKINGTON and many others see it, is to shift the focus of medical care back to the community and to lessen the emphasis on hospitals: "we want," he says, "a service for community health in terms of the family at home and at work, together with continuous study of disease and ill health within the community." And the obstacles, as he sees them, are not insuperable.

> "Nowhere in the world has the concept of a family doctor been more firmly rooted than in Britain. Nor have many countries been able to boast for so long a more complete cover of medical men trained in public health. . . . Why should we not now bring these two great institutions together? We have the means wherewith to solve our difficulties in a merger of public health and general practice."

At present medical care for people in their homes is provided partly by the family doctor, working in contract with the local executive council, and partly by district nurses, health visitors, home helps, and many other medical and social workers employed by local authorities. In BROCKINGTON'S opinion this division of domiciliary services between two separate administrative machines is quite unrealistic: "the general practitioner and the home nurse should work at least as closely together as the hospital consultant and the hospital nurse." As a professor of social medicine he evidently feels, too, that the family doctor's need of help from the health department is at least equalled by the health department's need of help from the family doctor. General practitioners should be the first and most important agents in public health.

> "Problems of care and aftercare, of the handicapped, of health education, the work of health promotion clinics, of immunisation and prevention of food-poisoning, of housing or such matters as the need to fluoridise the water-supplies, should concern them at every stage. We cannot afford to leave the general practitioner working alongside, but not as part of, public health."

He believes that the right place in which, and from which, the practitioner should work is a health centre, which could give him the scientific and the social instruments for a modern approach to health, and also the advantage of team-work—not merely in the form

1. Presidential address to the Section of Preventive Medicine.

of group practice but as a partnership of doctors with home nurses, midwives, health visitors, and home helps. "In uniting public health and general practice we could create something much greater than either separately," and the "new service for community care would become the friendly rival of the hospital service." One of its main objectives, indeed, would be to reduce calls on the hospital, and BROCKINGTON suggests that, except in emergency, it should be responsible for all admissions to hospital, which would enable it to give priority to those patients in greatest social need. The hospital would be used "as a very special instrument rather than a universal salve"; and apparently the bed bureau, besides procuring hospital admissions, would arrange for the domiciliary medical teams to give most attention to the people who require it most. As the senior administrative officer, the M.O.H. would coördinate the team, operate the bed bureau, and organise health education. "The records of medical teams and the hospitals, which should be made available to him, would guide the conduct of the community service. In this work he would be immensely aided by the closer association with general practitioners." The problems of community health would be under continual discussion by the doctors themselves in the local medical committee; and BROCKINGTON sets great store by the preservation intact of this statutory body, which has maintained the professional freedom of practitioners under the executive councils and could do the same under local government. "There would be no need to alter the present machinery for payment and appointments, and for dealing with the fortunately few complaints which arise."

One can agree with Professor BROCKINGTON's diagnosis without entirely approving his plan of treatment. In support of his proposal to transfer to local authorities the work now done by executive councils he can quote Sir JOHN MAUDE,[2] who considers such a transfer desirable as a first step towards administrative integration of our tripartite N.H.S. But the other members of the Guillebaud Committee differed from Sir JOHN about this and thought the suggestion would not commend itself to the medical profession.[3] If there were really such a thing as the "general-practitioner service" to which BROCKINGTON refers, the arguments for merging it with the public-health service might be unassailable; but in point of fact general practice is conducted not by a service but by individual doctors who have made a personal contract with individual patients. The provision of this kind of personal care is perhaps the main contribution of general practice to a world increasingly full of impersonal organisations; and we must beware of even so innocent and rational-sounding a measure as the "coördination of medical teams" should it seem likely to impair the family doctor's sense of personal responsibility. But if there is danger in the organisation of general practice by anyone other than the practitioner himself, it is also true that his patients nowadays often need the help of the various kinds of skilled people whom the M.O.H. can alone provide; and the Society of Medical Officers of Health is obviously right when it says that "medicine in the future can gain immeasurably from a development of collaboration between the general practitioner and the Medical Officer of Health and his staff."[4] How then can collaboration be further promoted? The general-practice review committee of the British Medical Association thought that "until there is at least a closer and more general administrative liaison between these two branches of the Service some difficulties and misunderstandings will persist."[5] The majority of the Guillebaud Committee, on the other hand, was not persuaded that changes in the machinery were the answer. "The problem of coöperation," they said, "has been tackled more effectively in some areas than in others and . . . where integration is lacking the reasons are probably to be found more in the personalities concerned than in any defects of organisation."[3] What is now needed most, we should guess, is more practical demonstrations of what can be done to improve the quality of general practice and public health by the collaboration of people who really care about both. This is the kind of invaluable experiment which does not necessarily depend either on health centres or on more money, but on vision and good feeling. Even a small merger by those keen enough to achieve it under difficulties could be more instructive than a large one imposed by statute; and we hope that Professor BROCKINGTON's arguments will lead many to think further about their local possibilities.

Treatment of Coronary Thrombosis

SCOTTISH institutions die hard, and the threat to the future of the *Edinburgh Medical Journal*, first published in 1805, has happily been averted by a union with the *Glasgow Medical Journal* to form a new *Scottish Medical Journal*. It is supported by the four Scottish medical schools and it is appearing monthly. The Edinburgh and Glasgow medical journals have in their day recorded the work and opinions of a great many famous men. In carrying on this task, the editor of the *Scottish Medical Journal*, Dr. ALEXANDER BROWN, and his colleagues have the good wishes of doctors in many parts of the world.

The first article in the first issue of the new journal deals with a subject that has engaged the attention of more than one Scottish medical school—the anticoagulant treatment of acute myocardial infarction. GILCHRIST and TULLOCH,[6] of Edinburgh, set out their views after seven years' experience which has convinced them that efficiently controlled treatment with oral anticoagulants has halved the death-rate during the first six weeks of hospital care; and they also believe that the incidence of thrombo-embolic episodes over the same period has been reduced even more. They point out the difficulties of obtaining really comparable treated and untreated groups of patients; but when proper precautions are taken and alternate cases are allotted to treated and untreated groups there is, they say, "a uniformity in the findings which is difficult to challenge." The mortality in a control untreated group from four large investigations works out at 29·2%, and the combined mortality for treated patients comes to 16·6%. In the seven years,

2. Report of the Committee of Enquiry into the Cost of the National Health Service. Cmd. 9663. H.M. Stationery Office, 1956; p. 285.
3. *Ibid*, p. 60.
4. Functions of the Medical Officer of Health. Published by the Society of Medical Officers of Health, Tavistock House South, Tavistock Square, London, W.C.1.
5. *Brit. med. J.* Suppl. Sept. 26, 1953, p. 145.
6. Gilchrist, A. R., Tulloch, J. A. *Scot. med. J.* 1956, **1**, 1.

GILCHRIST and TULLOCH have treated 321 patients with a mortality of 18·1% and an incidence of thrombo-embolic episodes of 10·6%. It is interesting to see that the mortality-rate has improved from 22·9% with the first dicoumarol-treated series reported in 1950 to 14·4% in the phenylindanedione-treated patients reported in 1954. With figures such as these, many people will wonder why anyone should oppose routine anticoagulant treatment for all patients; yet there is still much disagreement among cardiologists on this question.

The reason, shortly, is that the mortality of coronary thrombosis depends largely on the extent of the initial lesion, the shock it causes, the medical history of the patient, and the occurrence of subsequent thrombo-embolic episodes. RUSSEK and ZOHMAN [7] proposed an initial classification into "good risk" and "poor risk" cases, and they believed that anticoagulants should be given only to the poor-risk group, comprising about 30% of patients. In their experience the mortality-rate of untreated good-risk patients was only 2% and the incidence of thrombo-embolism less than 1%. Since anticoagulant treatment itself is not without risk, they argued, there appeared to be no good reason for using it for so slight an improvement. GILCHRIST and TULLOCH counter this view with several telling points. They say that the doctor is faced with the individual patient and his family, and if 2 or 3 in 100 good-risk patients can be saved by anticoagulant treatment when they would otherwise die, the slight risk is justified. Moreover, it is hard to judge, six to twenty-four hours after the onset of an acute infarction, whether the patient is, in fact, a good or a poor risk; and they quote the experience of HALPERN et al.[8] who found it necessary, within forty-eight hours of the onset of the attack, to revise the grouping of about a third of their series of 117 patients. But to delay a decision about anticoagulants for twenty-four or forty-eight hours is to deny a patient the benefits of early treatment. HALPERN et al. therefore gave every patient anticoagulants, but they stopped treatment after forty-eight hours in all those who could then be regarded as good risks. GILCHRIST and TULLOCH consider that this is too soon to stop treatment, and they recommend a minimum of ten days for the patient assessed as a good risk on the first day; should there be any unfavourable change, such as thrombo-embolism, the course of treatment can then be extended by three weeks. In the more severe cases they adhere to their previous recommendation of four weeks' treatment, extended if necessary by three weeks from the date of any subsequent thrombo-embolism. This programme means that *every* patient admitted to hospital is given anticoagulants, and this course can now be confidently adopted because the risk of therapeutically induced hæmorrhage has been so much reduced by present-day methods and drugs. GILCHRIST and TULLOCH, using phenylindanedione, with efficient laboratory control, have had no serious hæmorrhagic complications in their last 120 patients. If bleeding does occur, 10–50 mg. of the oral vitamin-K_1 emulsion will stop it.

GILCHRIST and TULLOCH also discuss other possible effects of anticoagulant treatment. They refer to the investigation of HELEN PAYLING WRIGHT and her co-workers [9] which showed that the rate of recanalisation of thrombosed arteries and veins is more rapid when the "prothrombin activity" of the blood is kept low. Another point is that pulmonary infarcts are much less frequent in patients who have had anticoagulants, even though the patients ultimately die; thus, in 88 treated but fatal cases, there were 3 pulmonary infarcts, whereas in 160 control necropsies in untreated cases, pulmonary infarcts were found 27 times—a striking difference. Prevention of pulmonary infarction is important because there is evidence, such as that provided by COLE et al.,[10] that these incidents diminish the immediate and later chances of survival.

The observations of GILCHRIST and TULLOCH, and all the arguments about anticoagulant treatment, concern, almost exclusively, those patients with myocardial infarction who are admitted to hospital for treatment. But not all patients with myocardial infarction are admitted to hospital; indeed, as MORGAN JONES [11] puts it, "it is very doubtful whether any community will in the future be able to provide enough hospital beds for the treatment of all cases of coronary thrombosis, even if this were desirable." MORGAN JONES reminds us that recovery is the rule if the patient is still alive when the doctor arrives. If the patient is still alive, then the decision to recommend removal to hospital or treatment at home has to be made; and this decision often turns on whether or not he needs anticoagulants. This brings us back once more to the assessment of prognosis, the decision between "good risk" and "poor risk." If the verdict is "good risk," then the relatively small advantage to be obtained from anticoagulants must be set against the risk of transport to hospital; if the assessment is "poor risk," then the patient should be got to hospital for anticoagulant treatment as soon as possible. The responsibility for this decision rests usually with the consultant called to see the patient, and he may be fortified by MORGAN JONES's opinion that "there must be few serious conditions in which we can at onset separate off clinically as large a proportion of cases with so hopeful and encouraging a prognosis." Thus, MORGAN JONES believes that good-risk patients can be treated at home without anticoagulants, and many cardiologists agree with him; but GILCHRIST and TULLOCH might not. The alternative is to give anticoagulants to all good-risk patients, comprising perhaps two-thirds of the total number; and to do so, some means must be provided for practitioners to get prothrombin-time estimated on blood samples taken in the patient's home. OWREN and others have used long-term anticoagulant treatment for myocardial infarction [12]; but in the domiciliary control of treatment from the start, blood samples must be collected at home and delivered to the laboratory and the result sent to the doctor as soon as possible. In his article this week, Dr. WATSON records his inquiries into the possibilities of organising such a service, with results that, so far, seem encouraging.

7. Russek, H. I., Zohman, B. L. *Lancet*, 1954, ii, 910; see also *Ibid.* 1955, i, 32.
8. Halpern, M. M., Lemberg, L., Belle, M., Eichert, H. *Ann. intern. Med.* 1954, **41**, 942.
9. Wright, H. P., Kubik, M. M. *Brit. med. J.* 1953, i, 1021. Wright, H. P., Kubik, M. M., Hayden, M. *Brit. J. Surg.* 1952, **40**, 163.
10. Cole, D. R., Singian, E. B., Katz, L. N. *Circulation*, 1954, **9**, 321.
11. Morgan Jones, A. *Brit. med. J.* 1955, ii, 1613.
12. See *Lancet*, 1954, ii, 742.

Annotations

A NEW MUSCLE RELAXANT

MUSCLE relaxants have so far been used mainly in anæsthesia, where a short duration of action and the need for parenteral injection are not disadvantages. A new preparation, zoxazolamine (2-amino-5-chlorobenzoxazole), is active by mouth and has a relatively long action.[1–3] It seems to act centrally and to depress the subcortical and spinal polysynaptic pathways. It has essentially no action on the monosynaptic arcs, motor nerves, myoneural junctions, or striated muscle. Zoxazolamine thus resembles mephenesin rather than the peripheral neuromuscular blocking agents such as tubocurarine or suxamethonium. Given to animals, zoxazolamine can produce a flaccid paralysis lasting several hours without a significant change in consciousness, blood-pressure, or respiration. Repeated daily, oral doses in rats and dogs produced no cumulative or toxic effects.

This new drug has been used in the treatment of spasticity caused by neurological disorders, and some preliminary reports have appeared.[4–6] Many conditions have been studied and the results have been variable. Clinical observation and electromyographic studies have confirmed that zoxazolamine is a mild muscle relaxant in some spastic states; but its action varies from case to case and even in the same patient at different times. Unfortunately reduction of spasticity does not necessarily mean improved voluntary control of limb movements, and it is often achieved at the expense of reduced muscle strength. A diminution in muscle tone has been noted, chiefly in patients with spinal-cord lesions; and this has been associated with abolition of uncontrolled mass flexion movements and considerable subjective improvement. The benefit in patients with spasticity of cortical origin and in paralysis agitans has been inconsistent and indefinite. The drug has also been used in patients with muscular stiffness and aching due to rheumatic diseases.[7] Side-effects have not been unduly troublesome with doses up to 0·5 g. four times a day. The commonest have been nausea, vomiting, epigastric discomfort, and dizziness. Fever and transient skin rashes have occasionally been noted. No blood abnormalities have been recorded.

There is no doubt that zoxazolamine has pharmacological properties as a muscle relaxant that make it suitable for long-continued administration. Chief amongst these are its effectiveness by mouth, duration of action, and low toxicity. But the benefit to be achieved by its use in spastic and rheumatic states cannot yet be assessed. Zoxazolamine can do nothing to the underlying disease, but by reducing spasticity it may aid physiotherapy and reablement. Conditions such as disseminated sclerosis and rheumatoid arthritis are notoriously variable in their course and this makes assessment of the drug difficult; and it seems itself to be rather irregular in its behaviour after oral doses. No further conclusions can be drawn on the evidence we have seen so far.

MENTAL DEFECT AND HYPSARRHYTHMIA

Prof. R. S. Illingworth [8] has described twelve children in whom severe dementia and convulsive disorders developed rapidly between the ages of four and eight months. The striking feature was an abrupt change in social responsiveness; motor and manipulative development were retained to a surprising degree. The initial fits were of various types, but later most of the children had salaam attacks. Neurological examination revealed no physical signs; but electro-encephalography showed the pattern which Gibbs et al.[9] call hypsarrhythmia. This pattern consists in bursts of very-high-voltage slow waves, together with spike activity which shifts rapidly from site to site: the abnormalities are diffuse, and normal patches of record are not found. The hypsarrhythmic pattern is common in young epileptic children with massive damage involving the subcortical masses.

The disorder described by Illingworth may be less unusual than is supposed because the characteristic epilepsy does not last long, nor does the E.E.G. pattern endure. One of the most striking features of the epilepsies of childhood is their sensitivity to maturation. Ounsted [10] has shown that the phenotypic expression of the convulsive genotype is rapidly overcome by maturation, and he has pointed out that this is true also of those epilepsies which go with hypsarrhythmia, and which stem from gross anatomical lesions: "The anatomical lesions remain; the mental defect remains; the characteristic E.E.G. pattern lingers on, but the fits themselves are inhibited by quite a slight advance in maturity."

Research into the epileptic diseases of childhood has been much neglected in this country. Children of the type that Professor Illingworth has described formerly died young. They now live on, a burden of hopeless pity to those who care for them.

TUBERCULOSIS AFTER PARTIAL GASTRECTOMY

DURING the past decade all too many defects have been attributed to partial gastrectomy; and it seemed that an increased incidence of pulmonary tuberculosis might prove to be one. Forsgren [11] was one of the first to show that after partial gastrectomy patients were more liable to pulmonary tuberculosis and that the risk to them might be ten times greater than to the general population. In this country Pulvertaft,[12] reviewing Visick's cases, found that of 23 intercurrent deaths from a total of 632 patients 7 had been due to pulmonary tuberculosis and 1 to tuberculous meningitis. Bruce Pearson [13] reported 11 cases, 4 of which were found in a follow-up of 93 patients; the other 7 were seen as cases of tuberculosis and could not therefore be measured as a proportion of a definite gastrectomy series. Tanner [14] was unable to demonstrate a prevalence of more than 5 per 1000 in the 403 patients submitted to mass radiography two to seven years after partial gastrectomy—the rate to be expected in the general public. But there were also 2 deaths from tuberculosis and 8 patients under treatment in the 611 consecutive cases of gastrectomy from whom the 403 were selected for mass radiography. These last figures are rather against Tanner's view that there is no increased proneness to tuberculosis. Allison [15] described 21 cases but gave no indication as to incidence; he suggested that "the faulty assimilation of nourishment together with metabolic imbalance brought about by chemical factors in the body, so lower a person's resistance that tuberculosis is a likely sequel in a certain proportion of patients." Thorn et al.[16] have now been more specific. They followed 955 patients in whom an X-ray examination of the chest was performed as a routine before partial gastrectomy, and they found that 6·3% had evidence of pulmonary tuberculosis before operation. In an admirable

1. Marsh, D. F. *Fed. Proc.* 1955, **14**, 366.
2. Kamijo, K., Koelle, G. B. *Proc. Soc. exp. Biol., N.Y.* 1955, **88**, 565.
3. Funderburk, W. H., Woodcock, R. T. *Fed. Proc.* 1955, **14**, 341.
4. Amols, W. *J. Amer. med. Ass.* 1956, **160**, 742.
5. Abrahamsen, E. H., Baird, H. W. *Ibid*, p. 749.
6. Rodriguez-Gomez, M., Valdes-Rodriguez, A., Drew, A. L. *Ibid*, p. 752.
7. Smith, R. T., Kron, K. M., Peak, W. P., Herman, I. F. *Ibid*, p. 745.
8. Illingworth, R. S. *Arch. Dis. Childh.* 1955, **30**, 529.
9. Gibbs, E. L., Fleming, M. M., Gibbs, F. A. *Pediatrics*, 1954, **13**, 66.
10. Ounsted, C. *Eugen. Rev.* 1955, **47**, 33.
11. Forsgren, E. *Svenska Läkartidn.* 1947, **44**, 1587; *Ibid*, 1948, **45**, 700.
12. Pulvertaft, C. N. *Lancet*, 1952, **i**, 225.
13. Bruce Pearson, R. S. *Postgrad. med. J.* 1954, **30**, 159; *Gastroenterologia, Basel*, 1954, **81**, 91.
14. Tanner, N. C. *Postgrad. med. J.* 1954, **30**, 523.
15. Allison, S. T. *New Engl. J. Med.* 1955, **252**, 862.
16. Thorn, P. A., Brookes, V. S., Waterhouse, J. A. H. *Brit. med. J.* March 17, 1956, p. 603.

study revealing the pitfalls which may trap those who make deductions from such an investigation (and also the means of avoiding them), they have proved that pulmonary tuberculosis is not related to the operation but rather to the standard of nutrition before operation. The attack-rate is high in men 15% below their standard weight before partial gastrectomy; contrariwise, if the preoperative chest radiograph and weight are normal there is little to fear. They point the moral: every attempt should be made before partial gastrectomy to raise the weight of undernourished patients, since the chance of restoring nutrition after the stomach has gone is remote.

CHILDREN NEED FAMILIES

FAMILY disruption undoubtedly contributes to juvenile delinquency. Evidence of this has been impressively adduced by Bowlby,[1] in confirmation of earlier workers, including Healy and Bronner[2] and the Gluecks.[3] Attention must therefore be given to the special problems of emotionally deprived children in any programme of delinquency prevention which claims to be comprehensive. This is the theme of a second report,[4] recently published by the City of New York mayoral office, with the significant title Children Need Families. The earlier New York report[5] dealt with broad preventive measures; the new one is concerned with the needs of children deprived of a normal home life. It emphasises the fundamental principle, in the rehabilitation of these dependent and neglected children, that they should be cared for on the basis of a family group.

The cornerstone of the New York programme is the provision of adequate numbers of suitably trained and professionally qualified social workers and counsellors, to augment existing child-welfare services within the city. Their chief rôle would be to conduct intensive field work among families otherwise likely to break up in disharmony. By providing close support and encouragement for emotionally inadequate, unstable, and often demoralised parents, the precarious family structure can be preserved and strengthened, thus reducing the load of emotionally deprived children for whom the community might otherwise become responsible. This is sound preventive medicine: it is also sound economics, since the cost of these expanded services is broadly balanced by the saving in keeping children out of trouble. When the family has already broken down, or when breakdown proves inevitable, the aim is to reinstate the child, wherever possible and as soon as possible, within his own family, by a sustained effort directed towards the parents, or, failing that, to find him at least a secure substitute home with enlightened foster parents, or parents by adoption if that is appropriate. This is, in essence, the reconstructive aspect of the programme. It is good to see the increasing recognition of these principles, and the decline of the earlier policy of accommodating such children in homes and institutions where their healthy emotional development was often endangered by the starched and impersonal atmosphere. As Mr. Epstein's report puts it, "children well fed, well groomed and clothed, substantially sheltered (in these homes), may still be miserable children. A chef in a stainless steel kitchen can hardly ladle mother love into the soup."

In this country, similar considerations are steadily gaining ground, as illustrated by the 7th report on the work of the Children's Department of the Home Office.[6] In London, the health committee of the London County Council proposes to employ some 50 additional whole-time home-helps, with the object of trying to keep together, at home, families whose children might otherwise have to be received into care, through illness or incapacity of the mother.[7] A proportion of these home-helps, after training, will also work with and teach housecraft to mothers who need help of this kind. As in New York, the aim is to prevent family dissolution rather than cater for its aftermath.

While applauding the expansion of these social services, we must temper our support with caution. The help given by welfare workers to families in need of readjustment and rehabilitation, involves encroachment upon emotional conflicts and intimate personal problems which demand tact, technical training, and enlightened understanding for their satisfactory resolution. It is of vital importance to ensure that the additional social workers to be recruited in this sphere have had the necessary training, and are imbued with a sense of responsibility that matches their rôle as home savers. Children do need families, but they must be stable and emotionally intact ones.

EKIRI

FOR a long time Japanese physicians and pathologists have been claiming that a form of acute infantile disease, *ekiri* (also known as *hayate* [typhoon] and as *kyusho* [acute illness]), though possessing many affinities with bacillary dysentery is not strictly speaking a shigellosis. As most of the work has been carried out in Japan it has not attracted much attention in other parts of the world. It has, however, aroused much local interest—so much so that a special study of it was made in the summer of 1947 by an American research team, and last April a symposium was held at Kyoto during the annual meeting of the Japanese Association for Infectious Diseases.

A report from Japan[8] on the ætiology of *ekiri* from the clinical, pathological, bacteriological, and biochemical aspects leaves many questions unanswered. The *ekiri* state, though acknowledged to be related to bacillary dysentery, resembles peripheral vascular failure due to anoxia in small children. Dembee Naito observes that the syndrome occurs only in Japanese infants; it is common among those aged 2–7, but no sucklings suffer from it. The syndrome consists in disturbances of the central nervous and circulatory systems in combination with disorder of the intestinal tract. It is thought to be due to some toxic product which acts mainly on the vascular system. It is stipulated that the toxin is non-bacterial—for instance, one of the toxic amines, which it is impossible to detect in the blood, though in the acute period there is a remarkable increase of blood-ammonia (0·84 mg. per 100 ml.). Amine formation is presumably due to the intestinal flora; the majority of tyramine-producing strains are *Escherichia coli* and *Aerobacter aerogenes*. Sakamoto and Suzuki assert that the syndrome is not fulminating bacillary dysentery. It is distinguished by intense circulatory disturbances. Sakamoto has brought forward evidence that it is a typical shock manifestation in response to a food allergy, for which he holds *miso*, a kind of soybean, responsible.

Despite the involved and often conflicting arguments it is difficult to escape from the suggestion that organisms of the dysentery groups are the chief factor. In Japan bacillary dysentery is widespread and severe; the fatality-rate in infants in the Kyoto Municipal Hospital, despite chemotherapy, is still over 10%. Confusion may have arisen because of the difficulty of culturing the dysentery group from the necrotic mucosa, where these organisms are swamped by other bacilli.

1. Bowlby, J. Maternal Care and Mental Health, W.H.O., Geneva 1952.
2. Healy, W., Bronner, A. New Light on Delinquency. Newhaven, Conn., 1936.
3. Glueck, S., Glueck, E. Unravelling Juvenile Delinquency. Cambridge, Mass., 1950.
4. Children Need Families. By HENRY EPSTEIN, deputy mayor, City of New York, Office of the Mayor, 1955.
5. Perspectives on Delinquency Prevention. City of New York, Office of the Mayor, 1955; see *Lancet*, Jan. 7, 1956, p. 34.
6. 7th Report on the Work of the Children's Department. H.M. Stationery Office, 1955.
7. See *Lancet*, Feb. 25, 1956, p. 307.
8. Advances in the Study of Ekiri in Japan. Edited by KAZUO OGASAWARA, M.D., professor of bacteriology, Nagoya University, Japan. Tokyo: Japan Society for the Promotion of Science. 1955. Pp. 101.

Special Articles

HEROIN
FROM THE INTERNATIONAL POINT OF VIEW *

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DIACETYLMORPHINE or heroin, the "wonder drug" of 1898, has been recognised, for several decades, as the most dangerous of the opiates—because it so easily induces addiction and because the treatment of that addiction can be so difficult and even perilous.

International Action

As long ago as 1923 the Opium Advisory Committee of the League of Nations proposed an inquiry into the suppression of this drug [1] but the main effort began with the conference which in 1931 prepared the Convention for the Limitation of the Manufacture of Narcotic Drugs. A group of four experts, including the late Prof. W. E. Dixon and myself, were asked a number of questions.[2] In reply we said that heroin was particularly likely to produce addiction because it is "more powerful than morphine and its dose is smaller," because "heroin euphoria is much more pronounced than that of morphine," and because troublesome "constipation does not occur in the addict". We regarded heroin as at least equal to morphine in its pain-relieving action, and as more effective in the relief of cough. But we also stated that its addiction-producing properties, from the medical point of view, are "much worse" than those of other addiction-producing drugs; we referred to the rapidity with which addiction is induced, to the change in personality with weakening of all the higher mental faculties, and to the difficulty of cure. We added that we had "evidence that a large majority of the eminent pharmacologists and physicians in various countries are definitely opposed to the employment of heroin in medical practice," and, when asked whether the drug is indispensable, we said that it "can be entirely dispensed with".

At this 1931 conference unanimity concerning abolition of the production, sale, and medical administration of heroin could not be reached; but Article 10 of the convention contained certain special restrictions on the export of heroin [3]—thus indicating the necessity for particular supervision—and the delegates passed the following recommendation [4]:

> "The Conference: Recognising the highly dangerous character of diacetylmorphine as a drug of addiction and the possibility in most, if not all, cases of replacing it by other drugs of a less dangerous character; Recommends that each Government should examine in conjunction with the medical profession the possibility of abolishing or restricting its use, and should communicate the results of such examination to the Secretary-General of the League of Nations."

Year by year the Permanent Central Opium Board and the Drug Supervisory Body (which started their work under the League of Nations and continue it under the United Nations) collected and analysed information on the licit movement of the drug—manufacture, import, export, consumption, &c.[5]; and in 1949 [6] and 1950 [7] the World Health Organisation's Expert Committee on Drugs Liable to Produce Addiction expressed alarm because production was still on the increase.

On the basis of the work of the expert committee and the information collected by the Director-General of W.H.O., the Sixth World Health Assembly in May, 1953, unanimously expressed its conviction that heroin is not irreplaceable for medical practice, and that the abolition of legally produced heroin by member States would facilitate the struggle against its illicit use. It accordingly recommended: first, that campaigns should be undertaken to convince doctors and governments that heroin is not irreplaceable, and secondly that member States which had not already done so should cease to produce or import the drug.[8]

Having received these recommendations, and also one from the Commission on Narcotic Drugs, the Economic and Social Council, on July 12, 1954, urged all governments to prohibit the manufacture, import, and export of heroin, and asked the Secretary-General of the United Nations to communicate this resolution to all Governments for such action as they might be in a position to take.[9]

The Response

How has the situation developed? Whereas in 1949 only 25 countries and 27 non-self-governing territories had given up the use of heroin in medical practice, of the 20 States which have still supplied estimates for heroin consumption in 1956 only 4—leaving aside for the time being the United Kingdom—are not prepared to renounce its use. As the World Health Organisation counts some 80 members, it is clear that the overwhelming majority of governments are in favour of abolition. The Expert Committee on Drugs Liable to Produce Addiction concluded last October "that more and more physicians throughout the world are finding it possible to substitute less dangerous drugs for diacetylmorphine, in accordance with the committee's repeatedly expressed view on the replaceability of this dangerous addicting agent".[10]

In the U.S.A., where the import, export, and production of heroin has been forbidden since 1924, the government maintains a small stock in case a doctor wants to administer this drug to a patient; but during all these years there have been only two requests for its use. In fact the American Medical Association never opposed the ban on heroin: rather they recommended its abandonment before the Act was passed. In 1917 the Council on Pharmacy and Chemistry of the A.M.A. deleted heroin from its *Handbook of Useful Drugs*, saying: "The Council holds that heroin has no advantage over morphine: that it shares every disadvantage of morphine; and that, on the whole, its introduction has been harmful, in that it furnished a specious means . . . for avoiding the well founded popular fears of morphine by substituting another habit-forming drug." In 1920 the house of delegates of the A.M.A. resolved: "That heroin be eliminated from all medical preparations; that it should not be administered, prescribed or dispensed; and that the importation, manufacture and sale of heroin should be prohibited in the United States".[10A] Although there have been sporadic expressions of dissent in the years since, there has never been any concerted move to restore the drug. Furthermore, contrary to rumours which apparently have spread in London, there has been not one request to the American

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* From a paper read in part to the Society for the Study of Addiction on Feb. 21, 1956. Author's present address is 1, rue de Contamines, Geneva.

1. League of Nations: advisory committee on traffic in opium. 5th session, Geneva, 1923; Minutes, p. 121. (Doc. C.418.M.184. 1923.XI.)
2. League of Nations' Conference for the Limitation of the Manufacture of Narcotic Drugs. Geneva, 1931. XI. 10; Records vol. 2, p. 129 (annex 7).
3. Text of the 1931 Convention as amended by Protocol of 1946. United Nations (1947, XI. 6), Article 10.
4. *Ibid.* p. 41.
5. Drug Supervisory Body Report (E/DSB/13). Geneva, 1955. XI. 3.
6. *Off. Rec. Wld Hlth Org.* 1949, **19**, 31.
7. *Tech. Rep. Wld Hlth Org.* 1950, **21**, 5.
8. *Off. Rec. Wld Hlth Org.* 1953, **48**, 22.
9. United Nations Economic & Social Council, E/Resolution (XVIII)/8, 1954, resolution G.
10. *Tech. Rep. Wld Hlth Org.* 1956, **102**, 5.

10A. *J. Amer. med. Ass.* 1920, **74**, 1324.

authorities in order to have heroin back. The A.M.A. is still vigorously opposed to its return.

In Germany, the heroin fatherland, it has not been used for a considerable number of years; it has practically disappeared from legal and illegal traffic alike. For the time being the drug is suppressed by administrative means in anticipation of a prohibition by parliamentary Act. The German Pharmacological Society and the Association of Chambers of Physicians have been consulted and have raised no objection.

No better illustration of the change of opinion can be given than that of Switzerland. At the 1931 conference the Swiss delegation declared that heroin was considered "indispensable for the treatment of certain diseases, in particular for certain cases of tuberculosis".[11] Twenty years later, however, Switzerland promulgated a new federal narcotic law in which the importation and manufacture of heroin, and trade in the drug, were prohibited.[12] This time, as the Swiss Federal Council stated in its message, the medical profession accepted the complete prohibition of diacetylmorphine.[13] Thus, although the same types of diseases have to be treated as twenty years ago, the medical profession can now do without heroin. Not one voice against this regulation has been raised in the Swiss medical journals, nor, as far as I could see, in the daily press. In the same message, the Swiss government said: "It should not be forgotten that the problem is of primary importance from the social and health points of view, and that in taking the initiative of this decision, the country will fulfil a humanitarian task which is in keeping with its traditions." There was no addiction to heroin of any importance in Switzerland which would have required suppressive measures, and the decision may have meant some commercial disadvantage since orders from foreign countries for other pharmaceutical products may be lost when the export firms are unable to supply heroin as well. This action by Switzerland therefore seems to me a particularly impressive example of international coöperation. Several countries where heroin has been abolished, retain a small stock of heroin for scientific purposes or for the use of any doctor who feels that in a particular case its administration is indispensable.

There are reasons to expect that at least one of the four countries which remain in favour of the use of heroin in medical practice will presently change its attitude.

British Opinion

I have followed with attention the development of the "heroin case" in Great Britain within the last few years, and particularly what has been written in the medical journals during the last fifteen months.

There is no doubt that, within the obvious limits set by public health, the doctor should be free to prescribe the drug of his choice: this is one of the necessary and fundamental rights in the conscientious practice of medicine. It is also clear that a drug which has been used for several decades to the satisfaction of many colleagues should not be abolished without the agreement of the medical profession. On the other hand, we all have some conservative tendencies in the use of medicaments. As has been mentioned, opinion has changed in Switzerland; and the same is true of Canada where it was formerly divided but where now (according to the Canadian delegate at the meeting of the Commission on Narcotic Drugs held in New York last spring) "the prohibition of heroin would not cause any difficulties in medical practice".[14]

When, on the recommendation of the British Pharmacopœia Commission, the monograph on heroin was deleted from the 1953 edition of the *British Pharmacopœia*, there was in the medical press no relevant discussion. When it became known in the House of Commons in February of last year that the Government intended to abolish the use of heroin from Jan. 1, 1956, the voices raised in the important medical weeklies were much less numerous than might have been expected.

The discussion at the annual representative meeting of the British Medical Association last June[15] showed, if I understood it correctly, that there was some misunderstanding as to the reason for the proposed abolition of heroin, although Dr. E. A. Gregg, the chairman of council, referred quite correctly to the dreadful picture of heroin addiction. Similarly, in some of the letters to the medical press doubt has been expressed whether the disappearance of heroin from medical practice would help in the suppression of illicit traffic of that drug. I am sure that it would do so, indirectly; for, as THE LANCET has said,[16] "the more countries that impose the ban the easier would be the task of those checking illicit traffic; for wherever the ban operates any heroin found is certainly illicit". But the World Health Organisation is not responsible for controlling the illicit traffic in drugs. It is a medical body and the purpose of its proposals was and is simply to try to prevent the *creation of heroin addicts in medical practice*.

The official figure of only 54 heroin addicts at present known in the United Kingdom is small—though it forms a fairly high proportion of the total of about 300 recognised drug addicts. It is not, however, negligible if I am right in supposing that at any rate the great majority of the 54 developed their addiction through therapeutic administration of the drug. Many of them, perhaps, would never have become addicts if they had been given another, less dangerous, drug instead of heroin with its great euphoric potency.

Reference has been made to "political pressure" from the World Health Organisation for the banning of heroin.[17] As a retired medical officer of W.H.O., I can say that no such pressure was ever in question. A resolution of the World Health Assembly, which is composed of delegates of the Member States, the overwhelming majority of whom are physicians or (if not) advised by physicians, cannot properly be characterised as "political pressure."

Alternative Drugs

What is quite clear from this correspondence is that some doctors still regard heroin as a most valuable drug for which there is no complete substitute.[18] One of them writes[19]: "It seems inescapable that many of the depreciatory remarks about heroin emanate from people who do not know its value, rather like the Russian gentleman who said whisky was not such a good drink as vodka because he had never tried it." For my part I should say just the opposite—namely, that many insist on the irreplaceability of heroin because knowledge of the alternatives is not yet widespread enough.

In discussing the possibility of replacing heroin fully by less dangerous (though also addiction-producing) drugs, we have to consider both its antitussive and its analgesic action.

Antitussive

Besides codeine and dionine, which are not always strong enough and can have undesirable side-effects, hydrocodone (e.g., 'Dicodid'), acetyldihydrocodeinone (e.g., 'Acedicone'), and dihydrocodeine (e.g., 'Paracodine') have been used for a long time. Among the

11. League of Nations' Conference for the Limitation of the Manufacture of Narcotic Drugs. Geneva, 1931. XI. 10; Records vol. I, p. 142.
12. Oct. 30, 1951, which came in force on June 1, 1952.
13. Message of the Swiss federal council to both chambers of parliament, April 9, 1951.
14. United Nations Commission on Narcotic Drugs, 10th session, 1955; E/CN.7/SR.263, p. 4.
15. *Lancet*, 1955, i, 1220.
16. *Ibid*, p. 1311.
17. Douthwaite, A. H. *Brit. med. J.* 1955, i, 907.
18. See, for instance, *Lancet*, 1955, i, 1220.
19. Mulvany, J. H. *Brit. med. J.* Jan. 14, 1956, p. 114.

recently developed drugs are methadone (' Physeptone ' linctus), pholcodine (which has to be classed with codeine), and dextromethorphan (known as ' Romilar '). This last product is said to have no side-effects, to maintain its efficiency over long periods, and not to induce addiction: it does not prevent the coughing up of phlegm or alter the consistence of the sputum,[20] and it has no analgesic action. It seems to be much used in the U.S.A.

Analgesic

Besides the more familiar drugs, such as hydromorphinone (' Dilaudid '), pethidine, methadone (' Physeptone '), and phenadoxone (' Heptalgin '), I should like to draw attention to levorphan (which in Great Britain formerly had the generic name methorphinan and is known as ' Dromoran '). In chemical structure it is closely related to morphine, but its analgesic effect lasts longer than that of morphine, and consequently much longer than that of heroin—which is helpful in the treatment of chronic pain. Its side-effects, including constipation, are less than those of morphine, and it also has the advantage of being effective when given by mouth. Other synthetic analgesics including pethidine and methadone are also effective by mouth but often cause nausea and vomiting, whereas levorphan is generally well tolerated. (For many years I have insisted on the need to avoid injection of analgesics, so as not to create a "needle habit" in potential addicts.[21]) At the New York session of the Commission of Narcotic Drugs in April–May, 1955, Dr. N. B. Eddy, chief of the section on analgesics, National Institutes of Health, Bethesda, Maryland, described levorphan as "as effective an analgesic as heroin" and "as effective as morphine in the treatment of cancer.[11 22] Therefore it seems to me that this drug deserves more consideration.

Conclusion

On a question so complex as that of heroin, there cannot easily be unanimity. Personally I have always recognised that in Great Britain there will be no danger to the public if heroin remains available in the future under the same conditions as at present. The British physicians and surgeons—probably mainly the older generation—who are accustomed to administering heroin, after surgical operations or otherwise, know how to manage this dangerous tool. On the other hand, reliable sources have repeatedly confirmed to me that the younger colleagues, as in other European countries, do not use heroin any more. Moreover, when it is given to relieve cough, there is no great risk that heroin addicts will drink whole bottles of linctus or cough mixture; for what they really look for is an intravenous injection or a chance to sniff their drug. If there were not a world-wide danger and an urgent request for coöperation by all countries—including the very few which have not yet agreed to abolish heroin—nobody would bother about the availability of heroin in the U.K.

On the other hand, the history of therapeutics has shown repeatedly that remedies held in great esteem are rejected when better ones have been found. I believe that heroin is now ripe for replacement.

I am hoping therefore that the British medical profession will agree to give up the use of this drug. I ask those doctors favouring heroin to re-examine the truly practical possibility of relieving extreme human pain without it. As the Home Secretary said last July, there is certainly a "need for an international effort to mitigate the heroin problem",[23] and in my view it is important to continue the efficient international coöperation over addiction-producing drugs which was started under the League of Nations. To abolish the use of heroin even where there is no national necessity to do so would be a valuable contribution to the idea that nations should work together for the common good.

20. See, for instance, Tünnerhoff, F. K., Schwabe, H. K. *Klin. Wschr.* 1955, **33**, 576.
21. Wolff, P. O. *Bull. Hlth Org., L.o.N.* 1945–46, **12**, 513, and earlier.
22. Eddy, N. B. United Nations Commission on Narcotic Drugs, 10th session, 1955; E/CN.7/SR.273, p. 8. See also Wolff, P. O. *Ibid.* 9th session, 1954: E/2606; E/CN.7/283, p. 15.
23. *Brit. med. J.* 1955, ii, 199.

NUTRITIONAL STUDIES IN A MENTAL HOSPITAL

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In general hospitals the turnover of patients is quick, and during their stay their diet often depends on their ailment. In mental hospitals, on the other hand, because patients stay longer, the diet is often even more important. We briefly describe here some of the results of nutritional studies at Claybury Hospital.

Material and Methods

During the greater part of this investigation patients in Claybury Hospital numbered about 2300, with a preponderance of females. About half of the women and a third of the men patients were over 65 years of age. The admission-rate is about 1300 per annum, and each year just over 1000 patients are discharged.

The main part of our investigation was carried out between May, 1951, and May, 1954. As far as possible we selected "ambulant" cases in apparently good physical health (all patients with recent feverish illnesses were excluded) who had been inpatients continuously for at least two years, but we also included some newly admitted patients.

A general nutritional survey was carried out during the whole time of the study, including control of nutritional intake and body-weight; and a larger proportion of the ambulant hospital population was regularly examined with special regard to symptoms and signs of early deficiency states (Leitner 1948).

All laboratory investigations were carried out after careful study of the case-history and after clinical examination. In many cases estimations were made of total carotenoids, vitamin-A reserves (Kimble 1939), vitamin-E reserves (Quaife and Harris 1944), vitamin-C reserves (Harris and Abbasy 1937), hæmoglobin level (Evans photo-electric hæmoglobinometer), prothrombin-time (Quick 1936), and petechiæ counts (Hess and Fish 1914).

The greater part of this investigation was carried out while essential foods were still rationed. At first we were tempted to follow the conventional quantitative food survey—to weigh and analyse sample meals and to deduct the remains on the plate. But apart from the fact that the resources were insufficient for such an investigation, we felt that it would only have specious precision; and singling out one particular ward for weighing and analysing meals for, say, a week might yield a misleading result as regards the hospital in general or even the selected ward in another week.

We therefore adopted a seemingly less exact method. The amount of food delivered to the central kitchen was carefully measured. Milk, meat and fish (fresh and made-up), and cheese were always weighed again before being sent to the wards. Fat and sugar were rationed; bread and potatoes were plentiful. Marmalade, jam, green vegetables, and fruit were scarce and they were therefore fully consumed. Our practice was to instruct repeatedly the ward sisters in several wards simultaneously to collect and preserve daily all the waste from the plates for consecutive periods of two to three weeks. The remains were carefully measured. We came to the

conclusion that only about 10%—rarely up to 15%—of the served food went into the pig-bin.

Results

Tables I–V summarise briefly the results.

Calories

The energy value of the average intake (table I) compares favourably with the recommendations of the British Medical Association (1950): 2750 calories daily for men on light work and 2500 calories for women, with 80 and 73 g. of protein. Incidentally our figures are slightly lower than those cited in the last report of the Ministry of Food (1953). Thus the calorie intake of the patients appeared to be satisfactory, and their diet contained sufficient animal and total proteins.

TABLE I—AVERAGE DAILY INTAKE OF FOODS PER PATIENT *

Month (1951–52)	Calories	Protein (g.)	Fat (g.)	Carbohydrate (g.)
October	2930	77	105	420
November	2800	73	98	406
December	2725	71	94	398
January	2700	71	93	393
February	2850	73	102	408
March	2775	72	99	399
April	2800	70	102	399
May	2745	71	101	388
June	2965	87	104	420
July	2770	72	99	397
August	2825	84	98	401
September	2875	76	101	415

* Calculated from all food delivered to the kitchen (after McCance and Widdowson 1946).

Hæmoglobin

The hæmoglobin estimations (table II), performed only as a sideline and always by the same experienced observer, show considerably lower values than those found by Olbrich (1947) for elderly people living in institutions (13·9 g. per 100 ml. for males and 13·2 g. per 100 ml. for females). It is perhaps pertinent to refer here to the many other causes of anæmia, such as chronic infection, occult bleeding due to peptic ulcer, colitis, and cirrhosis of the liver, which are so commonly found in patients with chronic ill health.

Prothrombin-time

A pilot survey of prothrombin-time gave normal values (table III) (normal clotting-time was standardised at 25 seconds).

Carotenoids and Vitamin A

As table IV shows, the level of blood-carotenoids in our patients was less than half that of other patients from London, and the blood-vitamin-A level was similarly much lower. Incidentally in 1945 we found similar low carotenoid levels in a boys' institution (Moore and Leitner 1949). On the other hand when 50 Claybury patients, chosen from those with the lowest carotenoid levels, were given daily a good helping of carrots or spinach (170 g.) their blood-carotenoid level was trebled within forty-four days, and the blood-vitamin-A level rose even higher than that of controls (Leitner et al. 1954). This demonstrated clearly that in certain aspects the hospital diet was far less satisfactory than that of the general population.

TABLE II—HÆMOGLOBIN ESTIMATIONS*

Group	No. of patients	Age (yr.)		Hb	
		Range	Mean	%	g. per 100 ml.
Males	178	16–89	59·5	82·3	12·2
Females	136	21–92	62·2	72·4	10·72

* Evans photo-electric hæmoglobinometer calibrated 100% = 14·8 g. per 100 ml.

TABLE III—PROTHROMBIN-TIMES

Group	No. of patients	Mean age (yr.)	Mean prothrombin-time (sec.)
Males	57	58·5	25·7
Females	19	61·4	27·7
Males and Females	76	59·2	26·2

Vitamin C

The vitamin-C status (table V) seems at first sight satisfactory. The gross average of the mean time necessary for saturation with ascorbic acid in our patients, from estimations throughout the year, was a little more than four and a half days. Only one similar investigation has been made in a mental hospital (Horwitt 1942), and in this the vitamin-C status was expressed as plasma-ascorbic-acid levels.* The comparison of results by these two methods is not easy (Prunty and Vass 1944), but our four and a half days' mean saturation-time certainly does not compare unfavourably with the low plasma-ascorbic-acid levels obtained by Horwitt in the U.S.A.

The purpose of the saturation test is to show whether the ascorbic-acid intake has been above or below some accepted standard of intake; and, if below, how much below (Harris 1943). We agree with Harris (1942) that in persons who are on the borderline of scurvy (or have scurvy) saturation usually takes seven to ten days.

In the Claybury patients the time needed for saturation varied widely, and this is consistent with the well-known seasonal variations (Harris and Olliver 1943). More than 10% of all our patients became saturated only on the seventh day of loading or later. In most cases this delayed saturation was found between March and July. A similar delay was present in our patients during three successive years. In fact of 117 men and 122 women patients examined during the "spring periods," 24 and 18 respectively fell into this group, while the corresponding numbers in 118 men and 103 women patients between July and March ("autumn period") were 2 and 4 respectively. Most of these patients with delayed saturation had obvious clinical signs of the scorbutic state. Nearly all had follicular hyperkeratosis with or without perifollicular hæmorrhages over the gluteal area,

TABLE IV—BLOOD-LEVELS OF CAROTENOIDS, VITAMIN A, AND VITAMIN E *

—	Patients in Claybury Hospital				Control patients		
	No. of patients	Mean age (yr.)	Mean stay in hospital (yr.)	Mean values	No. of patients	Mean age (yr.)	Mean values
Carotenoids (I.U. per 100 ml.)	179	59	16·5 (range 2–52)	88	220	45	219
Vitamin A (I.U. per 100 ml.)	159	,,	,,	118	219	,,	150
Vitamin E (mg. per 100 ml.)	175	,,	,,	1·15	64	,,	1·31

* Leitner et al. 1952.

TABLE V—ASCORBIC-ACID-SATURATION TESTS

Group	No. of patients	Mean age (yr.)	Mean body-weight (lb.)	Mean stay in hospital (yr.) (range)	Mean saturation-time (days)
Males	235	48·9	129·9	17·7 (2–44)	4·8
Females	225	52·6	125·6	11·0 (2–55)	4·5

on the outer side of the arm, or in the clavicular region; gingivitis and stomatitis with hypertrophy of the dental papillæ were common; but boggy, tender, bleeding gums were restricted to the few patients who had retained their teeth. Petechial hæmorrhages and ecchymoses, with extensive bluish purplish discoloration on the lower legs and ankles and occasionally on the forearms, were found in a group of male patients working in the gardens, but in none of the women who had a prevalently sitting occupation.

Petechiæ counts were performed in 278 of these 460 patients. As has been repeatedly noted (Medical Research Council 1953) the number of petechiæ was unrelated to the vitamin-C reserves.

Discussion

The nutrition of the patients in the hospital was such that gross deficiency states were uncommon. This is the more gratifying because several patients included in the investigation had been continuously at Claybury for fifty years or more. Only just over a decade ago, as many as 10 cases of frank pellagra were found in a few months in a single mental hospital (Hardwick 1943) (and 5 further cases were found within the same period in two general hospitals [Rimington and Leitner 1945]). During the present investigation only 3 cases of fully developed pellagra were seen; and 1 of these was in a newly admitted patient with florid scurvy.

While clinically obvious gross deficiency states were infrequent, detailed study disclosed "latent" deficiencies. In old people mucous-membrane changes are usually more or less readily detected; but skin changes, gingivitis in edentulous elderly patients with neglected mouths and with atrophied and shrunken structures, are more difficult to recognise, and they may occasionally be absent even in cases of advanced deficiency. Although the food was calorically sufficient and contained enough protein the nutritional status in carotenoids, vitamin A, and vitamin C was unsatisfactorily low, leading in many cases to deficiency states which were bound to impair general health.

The urgent need to reorganise catering arrangements in mental hospitals has been emphasised by Haringtion Hawes (1955). We support this timely proposal, although we are not convinced that fulfilment of such a programme would necessarily eliminate all the inadequacies found in the diet of our patients. We suggest that meanwhile the present scanty supply of vegetables (such as carrots, spinach, kale, leeks, turnip greens, tomatoes) should be enhanced by increasing the yield of the farms attached to many mental hospitals, and that each patient should be given routinely one 50 mg. tablet of ascorbic acid daily. We are aware that 30 mg. of ascorbic acid in the daily food provides a satisfactory margin of safety for the average person (League of Nations 1938). In mental hospitals, however, some patients, although without obvious symptoms and signs of disease, and perhaps only with occasionally recurrent mild attacks of diarrhœa or steatorrhœa, are far below average health, and may even be unable to absorb or to utilise nutrients satisfactorily (Boscott and Cooke 1954).

In our opinion any addition to the diet of a purified vitamin (such as ascorbic acid) is at best only a poor substitute for proper food, and this practice ought to be eliminated as soon as circumstances permit. But in our large mental hospitals we are faced with an unusually difficult and complex problem: many of the kitchens are old and their equipment obsolete; the financial allowance for food is limited; and often the patients, because of their mental disorder, are uncoöperative. Our studies have convinced us that even the most appetising diet will not be taken by some of these patients at all regularly without supervision and coaxing by specially allocated nursing staff. This supervision seems to be out of the question while the prevailing shortage of personnel persists, even if the financial resources were forthcoming. Addition of ascorbic acid seems to be the only immediate remedy for the poor vitamin-C intake in our mental hospitals.

Summary

A three-year nutritional survey in a mental hospital, combined with laboratory investigations, showed that the food provided sufficient calories; but the patients' hæmoglobin levels and their nutriture in carotenoids, vitamin A, and vitamin C were low.

It is suggested that all patients in mental hospitals should be given 50 mg. of ascorbic acid daily, and that the supply of leafy green vegetables should be substantially increased.

We thank Dr. J. S. Harris, physician-superintendent, for his help throughout this investigation, and Dr. George Graham for suggesting it. Our thanks are also due to the medical, nursing, and laboratory staff of the hospital, especially Mr. F. C. Radley and Mr. G. W. Swyers. The part of the work dealing with vitamins A and E was planned and carried out in constant coöperation with Dr. T. Moore and Dr. I. M. Sharman, to whom we are particularly grateful for much advice and help. Dr. Margaret Briggs, of Roche Products Ltd., kindly supplied the ascorbic acid needed in the investigation.

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FAMILY PLANNING ASSOCIATION

ON April 17 the Family Planning Association held in London an "Any Questions" meeting on Parenthood: by Choice or by Chance, with Mr. C. H. Rolfe, of the *New Statesman*, in the chair, and Mr. J. D. Bronowski, PH.D., Mr. Julian Huxley, D.SC., F.R.S., Lady Pakenham (who represented a Roman Catholic viewpoint), Canon Mervyn Stockwood, and Mrs. Mary Stocks answering the questions.

The questions ranged widely from the need for birth-control to combat the effects of death control to the ethical dilemma of the stage at which "interference" with reproduction might be allowed to take place. Most members of the panel thought that some degree of birth-control was inevitably necessary in all parts of the world, because the world population was increasing more rapidly than any possible increase in food production. With one exception they agreed that the discovery of a simple and infallible contraceptive would not be a danger to the human race. Dr. Bronowski thought that the birth-rate depended on the economic stability of a country, and the ability of parents to have a feeling of fulfilment in their children; when they felt able to do so they tended to have enough or more than enough children to maintain the population. Canon Stockwood

suggested that the urge to have children was too strong ever to be suppressed, and that easy and effective birth-control would simply enable a family or a population to cut its coat according to its cloth.

A lively argument arose over the morality of "artificial" versus "natural" birth-control. The panel agreed that birth-control should operate before, not after, conception, but disagreed on the permissible ways of preventing conception. Mrs. Stocks could not see the ethical difference between any methods of contraception once the motive of sexual intercourse with the deliberate intent of not having children was approved. To restrict intercourse to the safe period with this intent seemed to her to be no different from mechanical or chemical contraception at the same or any other time, except that it was less effective; it was the motive behind the act that was the key to the ethical problem. Lady Pakenham could not agree.

Doctors were hardly mentioned. The participants clearly held that the determination of national and individual policy on birth-control was the province of biologists, economists, statesmen, and churchmen. Mrs. Stocks thought that the doctors' job was to devise and disseminate contraceptives.

Symposia

THE NEUROHYPOPHYSIS

IN Michael Foster's textbook of physiology of 1894 it is stated that nothing is known of the function of the posterior lobe of the pituitary gland. By 1898 the gland was recognised to contain a vasopressor substance. Three years later Magnus and Schafer described the diuretic action of extracts, and in 1906 Dale noted their oxytocic properties. These facts were recalled by Sir Henry Dale in his opening address at the Colston Symposium on the Neurohypophysis, held in Bristol on April 9–12. The subsequent communications made it clear that the posterior lobe has not only three recognised functions—the control of water excretion by the kidney, of movements of the uterus during parturition, and of the ejection of milk as a result of suckling—but also almost certainly other just-glimpsed activities. In fact the posterior lobe may be one of the conductors of the endocrine orchestra of which the anterior lobe is the first violin.

The posterior lobe is part of a system which in vertebrates is old in the evolutionary sense, and which also has its homologues in many invertebrates. It is probably part of a neurosecretory system—i.e., the neurones manufacture active substances which are normally liberated from the ends of the axons. In invertebrates such as worms, crustacea, and insects a number of such systems are known; the secretions are stored in gland-like structures and are concerned with growth, metamorphosis, and reproduction amongst other functions (B. Hanström). In higher vertebrates the active substances are made in the supraoptic and paraventricular cells of the hypothalamus and are stored in the posterior lobe of the pituitary. There is evidence that the histological appearance of this hypothalamic/posterior-lobe system varies in the manner to be expected if the granular stainable material in the cells and their processes is indeed related to hormonal activity. The gland is equivalent to only part of the invertebrate system, so possibly other neurosecretory areas may exist (W. Bargmann). The form in which the hormones are present in the gland is not certain. The full activity of vasopressin and oxytocin resides in two octapeptides, but before release into the circulation these are probably attached to a large protein molecule which may be a "carrier" substance. Oxytocin may be removed from storage more rapidly than vasopressin, as is seen after parturition and during lactation; also, oxytocin does not appear to be made so early in life as vasopressin. Thus the two hormones show some measure of independence (C. Fromageot) and are remarkable for the apparent rate at which they can be removed from and rebuilt in the gland.

Excess of vasopressin is believed by some workers to be a factor in causing toxæmia of pregnancy. One difficulty in obtaining definite evidence for this view is that several antidiuretic substances can be extracted from blood, or formed from its proteins by enzymes natural to the body. These antidiuretic substances are not made by the posterior pituitary since they can appear in animals from which the posterior lobe has been removed (H. Croxatto). A further difficulty is that both vasopressin and oxytocin are so potent that they exist in blood in very low concentrations. Their estimation is a challenging problem. The obvious line of attack would be to collect blood flowing from the gland, since presumably there the hormone concentration would be at its highest. Owing to the situation of the pituitary this is more easily said than done, but in cavernous-sinus blood more oxytocin than vasopressin is found, which bears out the observation that oxytocin is the more mobile of the two hormones. There is a remarkable interchangeability between the hormones of different and widely separate species of animals; any oxytocin so far examined has always had the same chemical structure. Vasopressin is known in two forms. In most animals arginine is one of its amino-acids, but in the hog this is replaced by lysine. Hog vasopressin has far less antidiuretic activity in dogs than arginine vasopressin, but the other activities of the two types of vasopressin are equivalent (H. B. van Dyke). This fact may ultimately help to unravel the chemical processes whereby the antidiuretic action is triggered. The rate of disappearance from the circulation of injected vasopressin is rapid (about three minutes). Once released from the gland the hormones are destroyed by organs such as the kidney and liver, and they are also partly excreted in the urine (H. Heller). The estimation of vasopressin in the urine—usually as antidiuretic hormone (A.D.H.)—is one way of determining the conditions under which the endogenous hormone is liberated; thus it appears in greatly increased amounts in dehydration, fainting due to blood-loss, and emotional disturbances. A.D.H. appears in the urine of those suffering from motion sickness, but not of those who do not experience motion sickness, despite swinging and other stimuli; nor is it found as a result of blackout due to acceleration (R. L. Noble). Thus the pattern resembles that in many experimental conditions; an increase in the osmotic pressure of the blood, excitement, and certain types of volume or pressure change of the circulation, such as may be induced by changes in posture, induce antidiuresis.

There is little modern evidence that vasopressin ever, except during anæsthesia, has the vasopressor action which gave rise to the name it still bears. Accordingly it is generally believed that its power to raise blood-pressure is pharmacological rather than physiological; but, in rats at least, it may be a factor in causing compensatory vasoconstriction and maintaining blood-pressure after severe hæmorrhage (M. Ginsburg).

Closely allied to the question of polyuria is that of polydipsia, since in some conditions the former is primary and the latter secondary, or vice versa. It must be asked, therefore, whether there is a thirst centre comparable to the hunger and satiety centres which have been shown to exist in the hypothalamus. In goats electrical stimulation of defined areas in the anterior hypothalamus induces immediate and voluminous drinking, whereas destruction at certain sites produces complete adipsia. As yet it is not clear whether the drinking area is an entity in its own right, but it is possible to cause simul-

taneous drinking and antidiuresis owing to the overlap of the two regions (B. Andersson). Pituitary-resistant diabetes insipidus is known to occur in man, and for this reason among others it is of interest to discover just where in the kidney A.D.H. acts to cause water reabsorption. In the rat, urine can be collected by micropuncture from some parts of the distal convolution of individual nephrons. In all instances, whatever the concentration of the bladder urine, tubular urine from the first part of the distal convolution is hypotonic to plasma; the final process of concentration must therefore occur distal to this point—i.e., in the latter part of the distal convolution and perhaps also in the collecting duct (H. Wirz). A similarly hypotonic urine is found in the distal convolution of certain anurans which lack a thin segment of the loop of Henle, though the kidneys of these animals can concentrate under the influence of posterior-pituitary hormone (W. H. Sawyer). There is agreement, then, that concentration of urine due to vasopressin occurs in the distal part of the distal convoluted tubule, but it is uncertain whether concentration also takes place in the collecting ducts.

It is in relation to oxytocin that a number of new possibilities are appearing. So far this substance is known to affect uterine activity and milk ejection only, yet it is released from the gland in many circumstances and in greater quantities than is vasopressin; and it is normally present in the gland in equal amounts in males and females. It can be shown that the administration of oxytocin by itself may greatly affect blood-flow through, and sodium excretion by, the kidney and that when both vasopressor and oxytocic hormones are given together, in proportions in which they may well be released in the body, they have effects on sodium excretion not seen when either is given alone (F. P. Brooks and M. Pickford). It is unknown whether the action on the kidney is direct or dependent on an intermediary. For functional as well as anatomical reasons it is possible that oxytocin has some action on the anterior pituitary. For instance, although after parturition total absence of suckling allows mammary involution, in rats, if some mammæ are used and some are not, the unused ones do not involute, suggesting that suckling is the stimulus to a reflex release of prolactin which maintains alike the used and unused glands. Moreover, if oxytocin is given to rats with diabetes insipidus (i.e., with no endogenously produced oxytocin) the expected mammary involution does not occur. Suckling undoubtedly stimulates the posterior lobe to release oxytocin, which may then reach the anterior lobe via capillary vascular connections (A. T. Cowie and S. J. Folley).

Another important function of oxytocin may be in aiding the transport of spermatozoa from vagina to fallopian tubes. The known rate of movement of spermatozoa cannot account for the speed with which they reach the upper end of the genital tract; and there is good evidence for increased uterine movement in response to coitus. Now comes the observation of an apparent increase in the oxytocin content of jugular blood in cows when the uterus is stimulated manually. Taken in conjunction with the known action of oxytocin on the uterus, this suggests that coitus causes a reflex liberation of oxytocin which in turn induces coördinate movements of the uterus so that the sperms are swept rapidly along the genital tract towards the ovum (R. J. Fitzpatrick). Confirmation of this will depend on a suitable method for extracting oxytocin from blood, and there is some hope that a satisfactory method may be perfected. Already there are indications that oxytocin is present in jugular blood in greater amounts than vasopressin. This would agree with van Dyke's findings on the content of cavernous-sinus blood, and with the many functional studies which point to an always greater liberation of oxytocin than of vasopressin (J. M. Walker).

Finally, if the posterior lobe can influence the anterior lobe it may indirectly affect the adrenal cortex. Some link between them is suggested by the fact that certain types of stress known to affect the adrenal cortex at the same time deplete the posterior lobe of its A.D.H. Further, hydrocortisone seems either to speed the replenishment of the posterior lobe or to inhibit the release of A.D.H. In adrenalectomised rats hydrocortisone also protects the posterior lobe against the severe effects of dehydration (R. Gaunt, J. J. Chart, and C. W. Lloyd). There are still other pointers to the interaction of the posterior lobe and the adrenal cortex. Thus, an adrenalectomised rat with diabetes insipidus has an almost normal plasma-sodium concentration, but if the animal is treated with A.D.H. its plasma-sodium falls; and a rat with diabetes insipidus shows less loss of ascorbic acid from its adrenal cortex in response to a stress stimulus than does a normal animal, but it can be made to react in an almost normal manner by preliminary treatment with vasopressor posterior lobe extract (I. Chester Jones).

This is an impressive list of activities for a gland whose function was unknown sixty years ago. Recent work suggests that the list is by no means complete.

The whole symposium with the discussions is to be published as a book.

Occasional Survey

EOSINOPHILS AND THE SPLEEN

SINCE Paul Ehrlich described the eosinophil leucocyte as a distinct structure, a great deal has been written about this mysterious cell. The literature on this subject shows a curious shift of emphasis: earlier authors—for example, Ringoen [1]—were largely concerned with the phenomenon of eosinophilia; more recently, since the introduction of corticotrophin and the adrenocortical steroids, it has been eosinopenia which has attracted more attention. But some of the crucial facts about eosinopenia came to light fairly early in the story of the eosinophil. Ehrlich himself was already aware of the considerable decrease in the number of the blood eosinophils in "ordinary polynuclear leucocytosis," [2] an observation which led many European hæmatologists to regard the subsequent eosinophilia as the *Morgenrôte* of impending recovery from an acute infection.

As early as 1904, Opie [3] described eosinopenia in the guineapig under experimental conditions which today would be interpreted as "stress"; and Schwarz,[4] in 1914, and Borchard,[5] in 1928, drew attention to the rôle of the suprarenal glands in the production of eosinopenia. Yet it was easier to interpret eosinophilia in terms of a "positive chemotaxis," than to explain eosinopenia by "negative chemotaxis" [2]; and later work on the rôle of the eosinophil in protein metabolism [6] offered a key to the understanding of eosinophilia, whereas the observations on eosinopenia remained largely unrelated. Only when Dalton and Selye [7] noted eosinopenia in "non-specific stress" could these isolated observations be drawn together, and this finally led to the introduction of the Thorn test [8] (the response of the blood-eosinophil level to the administration of corticotrophin). The limitations and the usefulness of this test have recently

1. Ringoen, A. R. *In* Downey's Handbook of Hæmatology. London, 1938; vol. 1, p. 179.
2. Ehrlich, P., Lazarus, A. Histology of the Blood, Normal and Pathological. London, 1900; p. 144.
3. Opie, E. L. *Amer. J. med. Sci.* 1904, **127**, 217, 988.
4. Schwarz, E. Quoted by Best et al. (ref. 9).
5. Borchard, W. Quoted by Dustin and de Harven (ref. 15).
6. Biggart, J. H. *J. Path. Bact.* 1932, **35**, 799.
7. Dalton, A., Selye, H. *Folia Hæmatol.* 1939, **62**, 397.
8. Thorn, G. W., Forsham, P. H., Prunty, F. T., Hills, A. G. *J. Amer. med. Ass.* 1948, **137**, 1005.

been discussed by Best et al.,[9] Hench and Ward,[10] Thorn et al.,[11] and others. It is now becoming apparent that the adrenocortical steroids are not the only factors determining the level of the blood eosinophils: on the one hand, eosinopenia could be produced in adrenalectomised mice by injecting the plasma of adrenalectomised dogs [12]; on the other, "glucocorticoid" eosinopenia could be prevented by giving large doses of heparin.[13] But the response of the eosinophils to the administration of adrenocortical steroids can nevertheless be used not only as a method of assay,[12] but also to define the range of biological activity of new compounds. Thus, aldosterone is stated to have one-third of the activity of cortisone in the eosinopenia test,[14] whereas deoxycortone is inactive.[11]

It is apparent, therefore, that an explanation of corticosteroid eosinopenia might well help in understanding the mode of action of adrenocortical hormones. Several possible explanations have been advanced: Dustin and de Harven [15] suggest an inhibition of eosinophil production in the bone-marrow, and Gordon [16] considers that there is a direct effect on the circulating eosinophils; but recently another interesting hypothesis has been put forward by Esselier et al.[17] On the strength of experiments in which the reticulo-endothelial system (R.E.S.) was "blocked" by trypan-blue, they concluded that the "glucocorticoids" acted partly by inhibiting the release of eosinophils from the bone-marrow, and partly by increasing the extent of destruction of these cells by the R.E.S. The possibility that the R.E.S. was at least partly responsible had already been envisaged by previous workers (Thorn [18] for instance), and since the spleen is the most accessible part of the R.E.S., much attention has been paid to the relation between the spleen and the eosinophils. Biggart [6] refers to several workers who believed that eosinopenia is caused by overactivity of the spleen. An important observation was made by Opie [3] in 1904 when he noted that the spleen of the guineapig contained a considerable number of eosinophils, which were particularly abundant in the periphery of the pulp but were absent from the malpighian corpuscles. The more eosinophils there were in the circulating blood, the more there were in the spleen. When, however, the guineapig was starved for five to eight days, the number of eosinophils both in the blood and in the spleen was greatly reduced, but no decrease could be seen in the bone-marrow.

Opie's observations have been largely confirmed by later workers, but their significance was not fully appreciated for some time. In 1938 Klemperer [19] drew attention again to the fact that the spleen of reptiles, amphibia, and birds (he examined the flamingo) contained many eosinophils, as did the spleen of several humans of varying ages who had all died a sudden violent death; the number of eosinophils in the spleen was proportionately greater than in the circulating blood—partly owing, he thought, to selective migration from the blood-stream. Allen [20] and Enos et al.[21] have noted the disappearance of eosinophils from the human spleen when the patient survived some catastrophe, such as coronary occlusion, for a longer period. Enos et al. used the presence or absence of splenic eosinophils, in conjunction with changes in the adrenals and in the liver, to estimate the approximate survival-time of battle casualties in Korea.

This phenomenon has now been studied in greater detail by Sevitt.[22] By counting the number of eosinophils in sections of the spleen of people who had either died relatively suddenly or whose spleens had been removed within 3–7 hours of an injury, he established a baseline value for eosinophils in the normal spleen. The normal spleen contained many more eosinophils per unit volume than the blood, thus confirming the observations of Klemperer.[19] Within 24 hours, often even within 12 hours, of severe "stress" in the form of burns, infection, hepatic necrosis, &c., the number of eosinophils in the spleen fell progressively; splenic eosinopenia might then persist for several days. The accuracy of Opie's observations has thus been fully borne out half a century later.

By correlating the changes in the spleen with histological changes in the adrenal cortex and with the level of eosinophils in the blood, Sevitt found that splenic eosinopenia often preceded the loss of lipids from the adrenocortical cells, and that the splenic eosinopenia was in turn preceded by eosinopenia in the blood. Since the blood eosinopenia can, with certain reservations, be taken as a sensitive index of adrenocortical stimulation, it follows that splenic eosinopenia can be similarly interpreted. Splenic eosinophilia, however, does not necessarily denote adrenocortical failure. Caution is clearly required in drawing conclusions about a dynamic state, such as the life of the eosinophil, from a static histological picture; and Sevitt himself noted some apparent exceptions. Moreover, the depletion of adrenocortical lipids, the criterion used by Sevitt to denote adrenocortical activity, although useful, is nevertheless only an indirect index. As Symington et al.[23] have again pointed out, what is seen is variations in the lipid and not in the steroid pattern. Despite these limitations, however, it is possible to draw useful conclusions, as Sevitt and Enos et al. have shown, and it is probable that splenic eosinopenia, used in conjunction with histological changes in other organs, such as the pituitary and the adrenal glands,[24] will remain of interest and value, particularly perhaps to the forensic pathologist.

These observations also raise the question of whether the spleen plays an active part in the production of this eosinopenia—a question of great theoretical interest. At present no conclusive answer can be given, but certain experimental and clinical findings are relevant. The presence of necrotic eosinophils in the spleen suggested to Sevitt the possibility that this organ either destroyed viable eosinophils or removed degenerate cells from the circulation. Degenerative changes in circulating eosinophils had in fact been described in laboratory animals as well as in man.[16 25] Padawer and Gordon [25] considered that subsequent ingestion of these cells by the macrophages of the R.E.S. was the normal mechanism of disposal. Although the presence of neither the pituitary nor the adrenal glands is necessary for this destructive process, "stress" or adrenocortical hormones considerably enhance it. An accumulation of eosinophils, under the influence of cortisone, in the spleen of mice has been recorded by Spain and Thalhimer,[26] but the finding has not been confirmed in the rat.[27] The fact

9. Best, W. R., Kark, R. M., Muehrcke, R. C., Samter, M. *Ibid*, 1953, **151**, 702.
10. Hench, P. S., Ward, L. E. *In* Medical Uses of Cortisone, Hydrocortisone and Corticotropin. New York, 1954; p. 177.
11. Thorn, G. W., Jenkins, D., Laidlaw, J. G., Goetz, C., Dingeman, J. F., Arons, W. L., Streeten, D. H. P., McCraken, B. R. *Ibid*, p. 46.
12. Bibile, S. W. *J. Endocrin.* 1953, **9**, 357.
13. Godlowski, Z. Z. *Ibid*, 1952, **8**, 102.
14. Gaunt, R., Renzi, A. A., Chart, J. J. *J. clin. Endocrin.* 1955, **15**, 621.
15. Dustin, P. jun., de Harven, E. *Rev. hématol.* 1954, **9**, 307.
16. Gordon, A. S. Recent Progress in Hormone Research. New York, 1954; vol. 10, p. 339.
17. Esselier, A. F., Jeanneret, R. L., Morandi, L. *Blood*, 1954, **9**, 531.
18. Thorn, G. W. *Ibid*, 1950, **5**, 785.
19. Klemperer, P. *In* Downey's Handbook of Hæmatology. London, 1938; vol. 3, p. 1649.
20. Allen, A. C. *Arch. Path.* 1944, **37**, 20.
21. Enos, W. F., Beyer, J. C., Holmes, R. H. *Ibid*, 1955, **60**, 325.
22. Sevitt, S. *J. Path. Bact.* 1955, **70**, 65; *J. clin. Path.* 1955, **8**, 42.
23. Symington, T., Currie, A. R., Curran, R. C., Davidson, J. N. *In* The Human Adrenal Cortex. Ciba Foundation Colloquia on Endocrinology. London, 1955; vol. VIII, p. 70.
24. Currie, A. R., Symington, T. *Ibid*, p. 396.
25. Padawer, J., Gordon, A. S. *Endocrinology* 1952, **51**, 52.
26. Spain, D. M., Thalhimer, W. *Proc. Soc. exp. Biol., N.Y.* 1951, **76**, 320.
27. Fruhman, G. J., Gordon, A. S. *Fed. Proc.* 1952, **11**, 51.

that "glucocorticoid" eosinopenia can be produced in splenectomised individuals has convinced many workers that the spleen plays no part in the production of this phenomenon.[28]

That this conclusion may be an over-simplification is shown by the observation of Kresbach and Sailer [29] who noted that a significantly greater amount of corticotrophin was required to give a positive Thorn test in splenectomised animals than in intact controls. Similarly Sevitt, who compared the response in man of the blood eosinophils to corticotrophin before and 3–13 days after splenectomy, found that in some splenectomised patients an increase of the eosinophils preceded the corticosteroid eosinopenia, whereas in others the decrease in the eosinophils was greater than in normal controls. Although, therefore, the spleen may not be essential for the production of eosinopenia—presumably other parts of the R.E.S. can compensate for its absence—it cannot at present be entirely excluded from the mechanism.

Public Health

ATTENDANCE AT CHILD-WELFARE CENTRES

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THERE has lately been considerable discussion as to the present need for child-welfare centres. Not surprisingly, there has been some divergence of view, ranging from the belief that the day of these clinics is done, or at least that their scope should be severely restricted, to the conviction that the advent of the National Health Service has in no way diminished their importance.

While much of what has been said is speculative, many interesting facts have come to light as a result of interrogation of mothers by health visitors and by social workers.

Miller (1952) and others found that in Newcastle the artisan classes patronised the centres most, and that "poor" mothers, whose need for guidance was greatest, were less liable to attend than "good" mothers: only 1 mother in 5 attended regularly during a whole year.

Fisher (1953) believes that mothers prefer the clinic to the surgery because they dislike troubling the busy family doctor.

The survey conducted by George et al. (1953) in Birmingham and Cosely, Staffs, led them to conclude that one of the reasons for the attendance of 44% of mothers was the ability to purchase there proprietary foods cheaply; it was suggested that, while there was still a place for the local-authority clinic, the medical officer might well be replaced by a general practitioner.

Reed and Reed (1954) have called attention to the value of these clinics as a means of assuring mothers of children who attend for routine examination that their children are healthy. Their records of consultations with clinic medical officers show that advice (chiefly on feeding and skin conditions) was given in 63% of cases and reassurance in 27%..

Attention has been drawn to the fact that a large number of children attend the child-welfare centre once or twice only. In the Newcastle investigation (Spence et al. 1954) it was found that only 50% of the children attended more than three times during the first year, and there was a fairly regular fall in attendances after each visit; Spence et al. suggested that if the reasons for this fall could be found out, a great deal would be learned about what mothers needed, and how these needs could best be met.

Although in many places there is evidence that the number of mothers making use of child-welfare clinics has slowly decreased since 1948, there has been little to suggest that their popularity has really waned very much (*Lancet* 1954); indeed the introduction of a free general medical service has hitherto not had the notable effect that many expected. If group-practice becomes more popular, however, maternity and child-welfare clinics will be held increasingly in practitioners' surgeries, and the municipal-centre attendances will be undoubtedly affected; but the extent to which this will happen is highly uncertain.

The Report of the Ministry of Health (part II), 1953, emphasises the educational and preventive character of the maternity and child-welfare service, which is not an extension of the outpatient department for sick children; the need for these centres, with their emphasis on education, remains undiminished. The report points out, however, that there is much variation in the standard and method of health education, and that undue emphasis is often laid on the weighing of babies.

The value of child-welfare centres as part of a preventive mental health service has lately received increasing attention; many believe that there are great possibilities here, but it must not be forgotten that work in connection with problem families and maladjusted children has long formed an important part of the activities of clinic doctors and health visitors (L.C.C. Study Group 1954).

Questioning the public on health and other matters has become increasingly popular, and perhaps the answers given today lack some of the spontaneity and sincerity of those obtained when the public-opinion poll was first introduced. It may be objected that the replies given to general practitioners, health visitors, and social workers do not necessarily represent the true point of view of those questioned, but careful planning of questionnaires should in some measure offset this.

Plan of Inquiry

I describe here the results of an inquiry in two boroughs in South-East London, where, in addition to municipal clinics, many are organised by voluntary committees. The aim was to discover the views of mothers on the value of child-welfare centres, and their reasons for attendance or non-attendance.

The inquiry was conducted in three parts:

(1) A simple questionnaire was given to all mothers or adult females in charge of children visiting the centres during one week. Sealed ballot-boxes were used.

(2) In order to try to find out the attitude of mothers who did not make use of the municipal and voluntary clinics, a sample survey was taken in three new housing estates. The interviewers were preclinical medical students (Guy's Hospital).* "Lead-in" questions on health topics were included.

(3) Mothers who brought their children to the clinics on a few occasions only were asked to give their reasons for the poor attendance. They were sent a form which they were asked to complete and return to the health office.

Findings

REPLIES BY THOSE ATTENDING CLINICS

1361 persons replied to the questionnaire. To the first question—"what is the main advantage of attending a child-welfare clinic?"—the majority replied both "check on progress" and "for expert advice"; 37 said that they came for companionship, 128 to relieve anxiety (table I). Surprisingly, only about 16% gave the ability to buy foods cheaply as one of their reasons, but there were distinct differences in the replies from those who attended different types of clinics. In the voluntary centres in which proprietary foods were available on a lavish scale and a Ministry of Food clerk attended, this reason was given by 24% of mothers; the figure was 6·7% in the

28. Best, W. R., Muehrcke, R. C., Kark, R. M. *J. clin. Invest.* 1951, **30**, 629.
29. Kresbach, E., Sailer, S. *Klin. Wschr.* 1954, **32**, 742.

TABLE I—REPLIES BY 1361 WOMEN IN CHARGE OF CHILDREN ATTENDING CHILD-WELFARE CLINICS

Question	No.	% of total
Main advantage of attending:		
Check on progress	1018	74·8
Expert advice	926	68
Relieve anxiety	128	9·4
Better than doctor	36	2·6
Cheap foods, &c.	216	15·9
Companionship	37	2·7
Regular supervision	28	2·1
Can service be improved?:		
Yes	208	15·3
No	1030	75·7
Regular attendance?:		
Yes	1170	86
No	131	9·6
Reason for first attendance:		
Advice of health visitor	139	10·2
Advice of hospital midwife or antenatal clinic	77	5·6
Advice of doctor	9	0·5
Advice of neighbours, friends	42	3·1
Advice of foster-mother	7	1·0
First baby	219	16·1
Premature baby	19	1·4
To use service	63	4·6
Belief in child-welfare service	46	3·4
Mother's advice	10	1·0
Child not progressing	19	1·4
Vaccination or immunisation	7	0·5

council's clinics at which no Ministry of Food preparations were sold. No other specific statement was made by more than 10% of the respondents as a whole. Very few mentioned the general practitioner—2·6% said that the clinic service was better than that given by their own doctor.

To the fourth question—"reasons for first attendance"—the replies were few and varied: 16% said they first attended on the health visitor's or midwife's advice, and another 16% because they wanted help with their first baby. Otherwise only 1–2% of the respondents gave any particular reason, but many mentioned their ignorance as to how to bring up a baby.

On the third question 86% of the women claimed that they attended "regularly." In reply to this question, 136 reasons were given for not attending regularly (table II).

76% of respondents stated that the service could *not* be improved, while 15% said that it could. There was no appreciable difference in the replies from voluntary and

TABLE II—REASONS GIVEN BY 136 WOMEN FOR IRREGULAR ATTENDANCE AT CLINIC

Reason	No.
Only when requiring special advice	9
Child doing well	21
Child older	38
Ill health of mother	7
Other children	12
Children of school age	2
Mother at work	6
Less time	18
Child ill	8
Times inconvenient	7
Clinic too far away	4
First visit	1
Weighs baby at home	2
For first baby only	1
Total	136

council clinics; but, as was to be expected, criticisms were far fewer when the clinic was held in suitable premises than when a church hall was used.

Specific suggestions for improvement numbered 114 (table III); these suggestions were made, not only by the 204 respondents who said they thought improvement possible, but also by others who did not. The only suggestions made by more than a handful of respondents were: (*a*) more frequent sessions and longer hours (28 respondents); (*b*) more staff (20 respondents); and (*c*) less queueing and waiting (15 respondents). These suggestions would all seem to amount to the same thing, and while they can hardly be regarded as constructive in any detail they merit careful investigation.

SAMPLE SURVEY

A random sample of households was visited by the interviewers. Of the 306 respondents, 288 were mothers, 10 were fathers, and 8 were grandmothers.

The sample was obtained from the records of the housing authority, which gave the names and addresses of all the families in these estates with young children. Some 540 households were originally drawn as the sample; owing to the shortage of interviewers the final sample consisted of 382 names and addresses. Of these, 8% proved impossible to contact, 7% refused to answer because they were too busy, 2% had moved or were on holiday and in 3% of the cases there was no adult female or other suitable person present. This left 80% of the final sample, or 306 cases, as completed replies.

In answer to the question whether the respondent thought child-welfare clinics were a good idea, over 85% of respondents, both in those families where there were children under 5 years old and in those where the children were now older, answered "yes," and less than 15% "no." Of 198 *mothers* of children under 5 years of age

TABLE III—SUGGESTIONS FOR IMPROVEMENT OF CHILD-WELFARE SERVICE

Suggestion	No.
Open more frequently, longer hours	28
More friendly atmosphere, canteen, teas, &c.	9
More weighing-scales, less delay in weighing	7
More staff	20
Warmer premises	4
Less queueing and waiting	15
Better sanitation cleanliness	5
Better seating	3
More regular visits by health-visitors to homes	4
Stamps at food centres	2
Orange-juice to be paid for in cash	1
Children's old clothes to be on sale	2
Compulsory X-ray examination	1
Foot X-ray machine	1
Specialists from children's hospitals to attend	1
Sewing classes	1
Cheap foods at each session	3
Other	7
Total	114

who were questioned, 170 approved of child-welfare clinics; and of these, 115 gave reasons (table IV).

About 35% of all the *mothers* who responded (whether they approved of the clinics or not) thought it was worth while taking the children for expert advice. Only 5% said that their reason for approval was the opportunity to get a general check-up on the child's progress, and that it enabled them to get the child weighed; this contrasts with the 75% of mothers *at clinics* in the first part of the investigation who gave "check on progress" as their reason for attendance. 10% thought the clinic worth while for the inexperienced mother, which agrees with the 16% of attenders at the clinics who said they originally came with their first baby.

Thus 86% of mothers approved of welfare centres; but when they or the father or grandmother were asked

TABLE IV—REASONS FOR APPROVAL OF CHILD-WELFARE CLINICS NAMED BY 115 MOTHERS OF CHILDREN UNDER 5 YEARS

Reason	No.	Reason	No.
For advice	37	For welfare foods	7
For inexperienced mothers	11	Doctors are specialists	4
Weighing	10	Better than G.P. or hospital	3
General check-up	7	Hearsay	9
For first child	7	Other	20

TABLE V—CRITICISMS BY 43 MOTHERS

Criticism	No.
Risk of infection	16
Different views of people each week	4
Poor attention	4
Like to look after them myself	4
Long wait	3
Waste of time	3
Doctors rude	2
Never bothered	2
No faith in clinics	2
Interference	2
"Vague"	2
Do not agree with everything said	2
Not enough home visits	1
Prefer G.P.	1
Weighing only	1
"Too much messing about"	1
Did not get information required	1
Church hall too cold	1
No privacy	1
Ineffective	1
Put off by others	1
They want baby to grow up to their ideas	1
Some nurses better than others	1
Some nurses are poor advisers	1
Others	4

about frequency of attendance only 66% were prepared to say that the children had in fact been to the clinic.

This is probably an underestimate of the true proportion since they were replying to a question to establish frequency of attendance; possibly a reply was withheld in some cases, not because the children had never attended, but because the respondent was, in fact, uncertain of the frequency and did not care to say so.

As might be expected, the frequency of stated attendance and the time since last attendance (asked only of those with children below school age) diverged; 20% said that they attend or attended weekly and, of those who gave a date for their last visit 14% said it was a regular visit made under a fortnight ago. But whereas 67% said they attended monthly or more frequently, only 40% of those who gave a date for their last visit said it was a regular visit within the last six

TABLE VI—REASONS FOR DISCONTINUING ATTENDANCE

Reason	No.
Too busy with other children	26
Child well, visit considered unnecessary	18
Attending own doctor	16
Indifference to child welfare	13
Mother ill	11
Mother at work, grandparents looking after child	11
Distance to clinic too great	7
Too long a wait at clinic	5
Child ill	4
Satisfied with experience gained with older children	3
Unsatisfactory premises	3
Objection to advice given	2
Fear child might catch illness from other children	3
Child mentally retarded	1
Attends only to get help with child's clothing	1
Father a medical practitioner	1
Mother a nurse	1
Inconvenient day	1
Objection to referral to general practitioner	1
Fear and concern following death of first child	1
Did not want cheap foods	1
Difficult behaviour of older child at clinic	1

months. It seems, therefore, that the stated frequencies of attendance must be regarded with some scepticism.

Criticisms, totalling 62, were made by 43 mothers out of a total of 306 questioned; 12 had never been to a clinic (table v).

REASONS FOR POOR ATTENDANCE

Scrutiny of the registers at eleven child-welfare centres, selected at random, showed that in 1953 there were 2826 new attendances. Of these 248 came on three occasions or less, 145 (5%) once only, and 103 (3·6%) came two or three times. 58 had left the district, 14 were attending other child-welfare centres, and 6 were in day-nurseries.

The remaining 170 children (6% of all first attenders) were followed up by writing to the mothers and asking them to state in confidence their reasons for not continuing to attend. The replies (131) are classified in table VI. In 72 cases the reason for ceasing to attend may have been unavoidable (inability of mother to attend, or child ill or under care of general practitioner); and in 59 cases the reason was avoidable (mother did not consider further visits necessary, 38; criticism of premises or advice, 21).

The most significant point that emerges is the belief among a large number of mothers that, after the first baby, clinic attendance is not worth while unless the child is not making progress. Evidently, also, as the family increases in size, greater difficulty is experienced in finding time to visit. It is surprising that there were so few valid criticisms of the clinic premises or the attention received. Those who objected to the waiting-time were found on investigation to have grounds for complaint, but where the long distance to be travelled to the clinic was mentioned the complainants in no case lived more than a mile away. The infrequency with which the general practitioner was mentioned was unexpected; in 1 case the reason given for ceasing attendance was an objection to the child being referred to the family doctor. Needless to say the complaints made by mothers have all been followed up by the health visitors attached to the clinics concerned, and the complainants visited. These visits have confirmed the view that the majority of the criticisms had little foundation; but they have demonstrated the need for keeping in touch with those who do not attend regularly or cease attendance.

Conclusions

A large majority of mothers favour attendance at child-welfare clinics, because these provide a means of obtaining expert advice, checking progress, and relieving anxiety. It is apparent, however, that a large number do not think it necessary to visit if the child is making favourable progress, particularly in the case of subsequent children. Many mothers feel that the knowledge gained (generally at the clinic) with the first child, equips them to deal adequately with those that follow. Moreover the difficulties experienced in attending increase with the size of the family.

Ability to purchase welfare foods was not as significant a reason for attendances as might have been expected. It was found that at clinics where Ministry of Food preparations could be bought there had been very little increase in the number of clinic attendances. Weighing was not mentioned to any great extent, and treatment (and this is gratifying) not at all. The family doctor seldom figured in the replies, and preferences for the clinic or the surgery were fairly evenly balanced. Risk of infection was mentioned only by respondents who were questioned at home, and nearly half of these had never attended.

Those who frankly disbelieved in municipal clinics did not often give valid reasons in support of their objections, and criticisms even from unbelievers were few. Those relating to the staff or premises were found on investigation to have foundation in some cases; and for this reason, if for no other, the inquiry had some value. It also showed how essential it is for the health visitor to follow up all cases in which attendance ceases. It is a matter for surprise—and conjecture—that criticisms of premises were so infrequent, for many of these are far from satisfactory. Although most of the women claimed that they were regular attenders, there is a good deal of doubt as to whether this was a fact.

The demand for child-welfare clinics is as great as ever; but their value in the promotion and maintenance of health is insufficiently appreciated. For this the atmosphere of the clinic, if it has not changed with the

times, may be largely to blame. Undoubtedly there are considerable differences between clinics in respect of progress in health education and the use of visual aids and group discussions. This inquiry has, perhaps, suggested some of the ways in which improvements may be possible.

I acknowledge my indebtedness to Mr. T. David, formerly statistician to the London County Council, for the statistical analysis, and for planning and organising the sample survey. My thanks are due also to the medical students of Guy's Hospital who showed such keen interest and gave such valuable assistance, and to Dr. J. Crammond, late of the London School of Hygiene and Tropical Medicine, and to the health visitors and staff of Division 7, L.C.C. I am grateful to Dr. J. A. Scott, medical officer of health, London County Council, for his interest.

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Neonatal Mortality

In 1955 the neonatal-mortality rate in England and Wales was 17·3 per 1000 related live births.[1] This is the lowest annual rate recorded in this country; the previous record low rate was 17·7 in 1953 and 1954.

Parliament

QUESTION TIME

Maternity Services Inquiry

Replying to a question, Miss PATRICIA HORNSBY-SMITH, parliamentary secretary to the Ministry of Health, said that the members of the committee set up to inquire into the maternity services were as follows:

The Earl of Cranbrook (chairman); Mr. G. F. Gibberd, F.R.C.O.G.; Mr. H. J. Malkin, F.R.C.O.G.; Dr. A. Beauchamp; Dr. W. V. Howells; Dr. J. Forest Smith; Dr. Jean Mackintosh; Miss M. Williams, S.R.N.; Miss V. Shand, S.R.N.; Lady Pakenham; Mrs. Geoffrey Wilson; and Sir Basil Gibson.

Chairmen of Health Executive Councils

Replying to a question, Miss HORNSBY-SMITH, said that in England and Wales on March 31, 1956, 27 members of the medical profession were chairmen of local health executive councils.

Mr. CHARLES ROYLE: Does not the Minister regard the appointment of doctors as chairmen of executive councils as a rather undesirable practice? No education committee would appoint a teacher to the chairmanship. Will not the Minister make representations to executive councils along these lines?—Miss HORNSBY-SMITH: There are 13 lay and 12 professional members on such a committee and they elect their own chairman. If in special circumstances they believe that one of their number who happens to be a doctor, or for that matter a dentist, is outstanding for the chairmanship, they are free to elect him. Mr. ROYLE: Does that reply alter the principle?—Miss HORNSBY-SMITH: I think that the answer in many cases is that if lay members attended as regularly as some professional members, they would be in a better position to vote for someone else.

Mr. ARTHUR BLENKINSOP: Does not the hon. Lady appreciate that there is a point of substance here at which she might well look again? At the outset of the scheme the Minister appointed the chairmen. That was then changed. I think that it is highly desirable that executive committees should consider whether they should not appoint a lay person in many cases, unless there are exceptional reasons for the contrary. Miss HORNSBY-SMITH: The vast majority, of course, are lay chairmen.

Young Children in Remand Homes

Replying to questions Mr. W. F. DEEDES, under-secretary of State for the Home Department, said that the statistics of admissions to remand homes were not kept in a form which would enable him to say how many children were detained in such homes for truancy; and how many were detained between the ages of 8 and 11 years. These homes were used mainly for the temporary accommodation of children pending their appearance in court, or while arrangements were made for admission to an approved school.

Miss JOAN VICKERS: Does the Minister consider it desirable to keep children from truancy in remand homes? Last year in the home in which I am interested there were 55 such children. Will the Minister try to ensure that the younger children between the ages of 8 and 11 are not included in the remand homes with the older children who have committed many offences for which they have been brought before the courts on a number of occasions?—Mr. DEEDES: The second point in the supplementary question will certainly be borne in mind.

Prison Hospital Accommodation

Mr. FRANK ALLAUN asked the Home Secretary if he was aware that in the 88-year-old Strangeways Gaol, Manchester, prisoners confined to bed for long periods with tuberculosis had to be kept in the ordinary prison-cells, and that in the hospital of this gaol, holding 1100 prisoners, there were only four one-bed rooms for men who must be isolated because of mental or physical sickness; and what steps he proposed to take to provide adequate hospital accommodation in this prison.—Mr. DEEDES replied: The hospital at this prison is admittedly inadequate, but the only solution is to build a new one. This will involve substantial reconstruction of other parts of the prison, and will be undertaken when funds can be made available. The present accommodation in the hospital proper comprises three wards with thirty-two beds and four single rooms. In addition there is an extension of the hospital on one of the prison landings of twelve rooms. These are not ordinary cells but properly equipped hospital rooms with large windows. At present there are 5 cases of tuberculosis in the rooms on the prison landing. These cases are under the treatment of a tuberculosis specialist from outside, and are under the immediate supervision of the medical officers and hospital staff of the prison.

Mr. ALLAUN: Would the Minister agree that, whatever a man's prison sentence, his health should not be damaged by it? Will the Minister therefore ensure that sufficient hospital beds are made available at Strangeways for tuberculous patients and others with serious illness, particularly since, as I saw last week, it is extremely difficult for prison officers to carry sick prisoners into the four single bedrooms, two of them padded cells, because of the narrowness of these archaic corridors?—Mr. DEEDES: The difficulty is a structural one. The grounds of Manchester Prison are completely built up, and to build a new hospital it will be necessary to remove a branch of the prison to a site adjacent to the prison, which is now available.

Air-pollution Measurements

Replying to a question, Mr. J. R. BEVINS, as representing the Lord President of the Council, said that, under the ægis of the fuel research station of the Department of Scientific and Industrial Research, about 3000 measurements of air-pollution were made throughout the day and night during the fog, from Jan. 4 to 7 last, in the areas of London, Birmingham, Leeds, Manchester, Salford, and Sheffield. In the London area the averages of the results for pollution by smoke and by sulphur dioxide were about three-quarters of the averages during the severe fog of December, 1952, and between three and four times the concentrations in normal winter weather. The average concentrations of smoke and sulphur dioxide in the other areas of investigation were about the same as in the London area. The concentrations of carbon monoxide in the several areas were not much greater than in normal winter weather. The observations were made by more than 500 volunteers, including many from the Civil Defence Corps.

1. Registrar-General's Weekly Return for the week ended April 14, 1956. H.M. Stationery Office. Pp. 20. 1*s.* 3*d.*

In England Now

A Running Commentary by Peripatetic Correspondents

IN the book of elves and fairies beloved in my childhood, mental deficiency looked different from the problem which now I face.

The beautiful baby became a changeling—presumably through kernicterus or tuberculous meningitis—and lay brown, shrunken, and screaming in his cot till the goblins bore him back to fairyland. Nowadays the goblins' theft is often prevented by the cabbalistic rites of blood-replacement or intrathecal antibiotics, and the changeling remains, failing to gain weight, demanding and angry, dancing with rage because Earth has denied it honeydew.

In the Irish myths the plump, slow, creamy girls, or lads, with the eastern eyes were once the "lucky ones" who had either been blessed by the saints or had strayed as two-year-olds into the fairy ring, led by their slanting eyes and their "luck" into lonely adventures denied to others. They were laughed at, slow to learn, and loved music; they blundered but were tolerated. They too "joined the fairies" in childhood. as did our own mongols before antibiotics were discovered.

Others, who had been left in a fairy ring by a careless sister or brother in infancy, were less lucky, for they could nevermore escape its ceaseless dances. Charms were of no avail, nor even holy water, though sometimes a wise man guided their dance into useful ways, as we do with our spastics.

The book of elves and fairies led me astray, or the fairies have cursed the age of hydrogen. These are no longer the lucky ones. Today the changelings survive to rage and scream their way through the shrill echoing memories of their siblings. Mongols are no longer "blessed"; their childhood is not guarded by a spell nor their musical gifts used. The wicked fairy Pædiatrica stands by the cradle, and removes the normal spell of motherhood. "You have borne a monster—a mongol—hide it from the sight of other children lest they be afraid." I wouldn't mind this so much if Pædiatrica would wave her wand until the long waiting-list for mental-deficiency institutions had vanished. Instead, like all wicked fairies, she disappears immediately in a puff of smoke, pocketing a domiciliary fee, or pontificating to the apprentices.

I wish you would go away, or stop your charms, Pædiatrica; and, pending more green hills for changelings, give the peculiar-looking baby a chance to turn out "lucky" at home.

* * *

A Cockaignshire local medical committee has been hearing an interesting case. Dr. X, a local practitioner, was asked why he had prescribed, on an E.C.10, a stone of dog-biscuits.

Dr. X explained that the patient, Mr. Y, believed himself to be a dog, and was under the care of a Psychiatrist who insisted that he be humoured and prescribed certain tablets. The only way to get Mr. Y to take the tablets was to conceal them inside small dog-biscuits. Dr. X contended that the dog-biscuits were therefore not a food, but an ancillary medicament or vehicle, the equivalent of a syrup or flavoured water. If the Chairman thought he could talk Mr. Y out of his delusion (said Dr. X), he was welcome to try; but so far Mr. Y had proved unusually intransigent. Indeed, after his last session with Mr. Y, the Psychiatrist had suddenly tied a small barrel under his chin and crawled out howling into a snowstorm.

Dr. X claimed that his duty not only as a doctor but also as a citizen demanded that the patient be kept fit for work; for Mr. Y was a key man. He made the tea for the men who made the tea at the Ministry of Incoördination in Ataxia House. He was irreplaceable also in that he was left-handed, and nobody else could use his peculiar left-handed teaspoons. The Committee would be aware from the Press (continued Dr. X) that there was a crisis over the question of pay-differentials between right- and left-handed tea-stirrers, and he would ask the Chairman whether the national economy was to be endangered for the price of a stone of dog-biscuits.

Dr. X spoke for a further 45 minutes on the Englishman's love of animals, concluding by singing several verses of a ballad entitled, *My Four-legged Friend*, and inviting the Committee to join in the choruses. But the meeting had to adjourn, owing to the indisposition of the Chairman, who felt his nose becoming hot and dry.

* * *

The last patient at the clinic was a woman with neurodermatitis. The boss was evidently tired. He had reached the critical point at the end of the afternoon when his mind would accept nothing but the most relevant remark through its fatigue barrier.

"Now ma'am, you have had your skin trouble for how long?"

"For thirty years at least. I have seen most of the dermatologists in the country, and none have done me any good."

"And what makes you think we will succeed where they have failed?"

"I had heard you were supposed to be good at this sort of thing."

The boss closed his eyes and breathed deeply. Anyone who did not know him would think he had fallen asleep. I knew he was wrestling with his serpent.

"Tell me, ma'am. do you use nail varnish?"

"It seems rather a personal question, but if it is of any interest to you, I don't. My nails are naturally highly polished.

"Naturally. And do you scratch?"

"Never! Dr. Smyth accused me of that. It simply isn't true. I want to scratch but I am able to control myself."

"Indeed. How long have you had your eczema?"

"Is that what it is! Then why do they call it dermatitis . . . every specialist that I come to has a different name for it. I do wish someone would explain to me in simple language what I have got and how to cure it."

The boss turned slowly on his swivel chair and addressed me as though we were alone together.

"Not so easy, Peter. How does one explain in simple language that this skin lesion is a localised area of unhappiness, a focus of frustration? It is a flag she is waving, but whether for help or in warning it is difficult to decide. This patch of eczema is a target on which she receives the slings and arrows of outrageous fortune: though, here again, if fortune is outrageous we are so often ourselves the cause of it being so. And she has, of course, scratched and scratched and scratched continuously for thirty years to sustain it . . ."

"Do you mean to tell me that I have deliberately kept it going? It's ridiculous!"

". . . to sustain it for fear of losing it."

"Well, it is obvious that I am not going to get any help from you! It was a waste of time coming."

His voice lost its edge and I knew the physician had begun to rewind the serpent round its staff.

"Sit down, dear lady, and relax a little. I am sure we can help you. We will give you a paste and the rash will improve . . ."

"I have heard that before."

". . . if you don't scratch. I shall also dispense for you some medicine."

"Is it brown? I've had it! It never did me any good—only upset my stomach!"

"I shall dispense some bromide and nux vomica. This is *not* brown but red like claret."

The boss took my arm and led me out of the cubicle.

"Peter, I would like to see this patient again in six weeks, when I hope to prove to you that there are some skins that we have no right to cure if we have the comfort and happiness of our patients at heart."

I took a swift look to see if he was smiling. If he did smile it had already gone; but he did not look quite so tired.

* * *

News from School.—The music comp. was very good. The pianos were never together. Even the recorders were not together, let alone being in time with the pianos. Everybody was stiffling their laughter. — House had cellos, violons, and viola, but people say it was not a match against last year's, as it was not nearly so out of tune.

Letters to the Editor

DEFICIENCY OF ESSENTIAL FATTY ACIDS

SIR,—Dr. H. M. Sinclair's engaging essay in your issue of April 7 merits more detailed comment that I can supply at this distance from my home laboratory. However, some notes may help your readers appraise the situation in a field unduly beset with conflicting claims and feverish competition.

Besides solving the coronary heart-disease problem, Sinclair disposes of lung cancer and leukæmia for good measure; but these latter minor problems I shall leave to others. The central issue of Sinclair's speculations is atherogenesis and the regulation of the concentration of cholesterol in the blood. His thesis is that our present plight in Britain, the United States, and other countries where coronary heart-disease is so alarmingly frequent, is due to dietary deficiency of the "essential" fatty acids—linoleic and arachidonic—largely ascribable to the evils of hydrogenation and deficiencies of vitamin E and pyridoxine.

While I join in deploring the increasing use of hydrogenation and many other methods of "improving" our natural foods, I think it can be shown that even in the United States hydrogenated fats are only a small fraction of the total fat consumption, which provides, moreover, a per-capita intake of linoleic acid at least as high as that of many populations, as in Japan, who suffer relatively little coronary heart-disease.

The idea that a deficiency of essential fatty acids (E.F.A.) in the diet may be related to atherogenesis is not new; it was suggested a dozen years ago by Dr. George Burr, then at the University of Minnesota, and it has been discussed in the United States for several years, notably by another Minnesotan, Dr. Ralph Holman of our Hormel Institute. Last year Dr. B. Bronte-Stewart developed this thesis in South Africa and recently he discussed the question in England. It is well known that animals fed diets extremely deficient in E.F.A.—and such diets are not easy to prepare—often have increased amounts of cholesterol in the liver, but I know of no demonstration of the production of atheroma in these experiments. Moreover, I am unaware of any evidence that a low intake of E.F.A. in the human diet will, by itself, produce either hypercholesteræmia or atherosclerosis. Indeed, even the possibility of E.F.A. deficiency in adults is debated vigorously, and there is not yet unanimity of opinion about the situation among infants, where the best case for the essentiality of E.F.A. has been made—by another former Minnesotan, Dr. Arild Hansen.

It is easy to show, as we have been doing for half a dozen years in controlled experiments on man, that merely changing the proportion of calories supplied by ordinary food fats (not hydrogenated) in modern Western-type diets promptly results in corresponding changes in the serum-cholesterol concentration, even when the intake of calories, cholesterol, proteins, and vitamins is constant. In such experiments, each lasting from four to six months and involving twenty or more men, isocaloric substitution of carbohydrates (sugar, potatoes, and bread) for a large part of the dietary fats involves a sharp reduction in the intake of E.F.A.—and the serum-cholesterol falls and stays down so long as the low-fat diet is continued. But when the reverse substitution is made, using lard, butterfat, cottonseed oil, olive oil, coconut oil, or mixed food fats, the serum-cholesterol concentration rises. Supplements of vitamin E or of protein (casein) do not alter the result.

These several food fats do not produce quantitatively the same degree of elevation of the serum-cholesterol, and a few fats, which do not bulk large in our diets, may have no cholesterogenic effect. We have observed this as well as others, including Kinsell in California, Ahrens in New York, and, recently, Bronte-Stewart in South Africa. But the point for the present discussion is that with most of the common food fats an increase in the fat consumption produces an elevation of the serum-cholesterol at the same time the intake of E.F.A. is being increased.

Now it is conceivable that E.F.A. may have no cholesterogenic effect and that large amounts of E.F.A. may counter some of the cholesterogenic tendency of fats containing no E.F.A. But even if this were true it seems unreasonable to ascribe to a "deficiency" of E.F.A. the result of increasing the total intake of fats *and* of E.F.A. (for none of our ordinary food fats are devoid of E.F.A.). I believe it is difficult to ignore the impressive body of evidence leading to the conclusion that our present prevalence of hypercholesteræmia and coronary heart-disease would be much altered if we simply reduced the general level of fat in the diet, and that we got into our present plight, at least in part, because we have adopted an increasingly fat-rich diet. We are rapidly approaching the time when we must ask seriously what is to be done about it. Dr. Sinclair's argument obviously suggests that we solve the coronary problem, without retreating from our high-fat diet, by taking a daily swig of linoleic acid and a few vitamin pills. I wonder whether this is a responsible answer to a serious question.

There are other difficulties with Sinclair's thesis and the facts he adduces in its support. He indicates that Eskimos and "some Norwegians" consume high-fat diets but escape atherosclerosis because they eat marine foods in a diet unsullied by the chemist. He forgets that recently [1] he argued persuasively that Eskimos have long since ceased to eat high-fat diets. And he seems to be unaware that large amounts of hydrogenated whale oil are eaten in Norway, which is, nevertheless, not among the countries eating the largest amount of fats. (The latter are, more or less in order of decreasing fat as a percentage of total calories: U.S.A., Finland, Australia, New Zealand, Denmark, Canada.) In any case no-one knows what may be the freedom, if any, of the Eskimo from atherosclerosis; it *is* known that coronary-heart disease is a serious problem in Norway.

Sinclair makes a good deal of cholesterol esters as the villain in the piece. Two facts should give pause here. In the first place, pathologists tell us that the cholesterol esters, as a fraction of the total, are relatively low in newly formed atheroma and that the percentage of esters rises with the age of the lesion. And in the second place, the proportion of ester to free cholesterol in the serum is substantially the same in hypercholesteræmia as in normal or hypocholesteræmia, in coronary patients and in their clinically healthy controls. Further, the amount of cholesterol esters in the liver and in the skin may be interesting, but I do not know that anyone has suggested this as a measure of atherosclerosis.

I feel strongly that a most important clue to the solution of the coronary problem is in the differing frequency of the disease in populations that differ in their modes of life. And I am pleased to learn that Dr. Sinclair is agreeing with me that the diet plays a most significant rôle in this. Consideration of the dietary fat and the rôle of cholesterol in the blood transport of this (as lipoprotein) seems to resolve the striking contrasts in the burden of coronary heart-disease we have observed in comparing Americans and some Europeans with southern Italians, Sardinians, African Bantu, and Japanese on their native diets. Climate is not the answer, and no more than a minor rôle can be given to the frequency of obesity in the several populations. If serum-cholesterol is the criterion, dietary fat far outweighs differences in physical activity as a causative factor, and we observe that there are plenty of physically inactive men in Italy and here in Japan but

1. *Proc. nutr. Soc.* 1953, **12**, 69.

still coronary disease is relatively uncommon in these populations. Finally, there is no evidence that race is involved and a good deal of evidence that it is not, notably in comparisons between Negroes in Africa and in Chicago, in comparisons between people in the same region who differ in their economic circumstances (as found in our studies in Spain and in Italy), and in our current comparisons between Japanese in Hawaii and here in Kyushu. But in all of these situations attention to the total fat in the diet seems to bring an orderly relationship into focus.

Probably no such clear and simple relationship would be found if the dietary predilections of the world's populations for quantities and kinds of fats varied independently. I should not expect to find the same serum-cholesterol levels and frequencies of coronary heart-disease in two populations both getting 40% of their calories from fats but the one deriving this from corn oil and sesame-seed oil while the other got all their fats from coconut oil and lard. But this does not happen to be the way people consume fats. In a desperately poor land the people get very few fats of any kind. As their lot improves economically they increase their total fat consumption, *and* the fats they eat tend to be more and more the more expensive kinds—the fats that, incidentally, are associated with the foods most highly prized for their nutritional as well as their gustatory value.

To some of us, at least, it appears that this response to prosperity can go too far. The problem has been complicated by the enterprise and ingenuity of food producers and technologists who provide a super-abundance of all kinds of fats and then persuade us to eat them. Are we now going to ask them, please, to put some more E.F.A. in their wares? Perhaps with a modest increase in cost? This could be the shape of things to come. Continue, or increase, your high fat consumption but be sure you get a lot of corn oil, sesame-seed oil, fish oil, and the like and be careful to swallow it fresh and in the virgin liquid state!

Such considerations may seem inappropriate in a discussion of a problem that is basically chemical and pathological. But the coronary problem has already reached dimensions that cannot be confined in the other-worldly atmosphere of some academic retreats. In the meantime, it is clear that a great deal more research is needed on all aspects of the problem, including food economics and the psychology of food preferences. While this is in course it may be well to ponder whether a diet containing 40% of its calories as fats is really essential for human happiness and, if not, how may it best be reduced.

First Medical Clinic,
Kyushu University Medical School,
Fukuoka-shi, Japan. ANCEL KEYS.

VOMITING SICKNESS IN JAMAICA

SIR,—There are two important points which might be added to your leading article (April 14). As far as I know, chemical analysis has not yet been published to indicate in what part of the ackee fruit the toxins are found. If they are only in the seed, then the population can continue to eat the arillus with impunity. Children who eat the seed in play, or tragically driven by hunger, must be more carefully supervised. The other point is quantitative: not only which part, but how much of which part, of the fruit is likely to produce a toxic effect.

The full report of the work done in 1952–53 (excepting the chemical section) was published by the Government Printers, Kingston, Jamaica, in 1954, as a monograph on Vomiting Sickness in Jamaica.

London School of Hygiene and
Tropical Medicine, W.C.1. CICELY D. WILLIAMS.

REVISION OF THE CURRICULUM

SIR,—The only positive contribution in the proposals of the Royal College of Physicians anent revision of the medical curriculum is the suggestion that the G.M.C. should cease to issue recommendations—in other words, abrogate its function as guide and supervisor of the training of medical students. Otherwise the report (of which extracts appeared in your issue of April 14) consists in the usual ponderous, pontifical pronouncements that the aim of medical education should be to give "a broad cultural background," "the acquisition of a scientific attitude," "principles and outlines without the burden of fact," &c., &c. We have heard most of it before in the perennial bellyache about the medical curriculum which is a perpetual item on the agenda of committees of medical schools and Royal colleges and corporations, in fact of every conceivable body except those best suited to advise—namely, the general practitioner. No other training schemes—for lawyers, engineers, scientists, &c.—are subjected to so much interminable "research." Quite obviously the present training of the medical student is unsatisfactory, uneconomic, and much of it wholly irrelevant to the work subsequently undertaken by the great proportion of medical graduates.

Medicine is not a philosophy, nor is it a science. It is a skill, much of it still empirical; and, like training for any other skilled job, the education of the medical student should include, from an early stage, a concurrent and remunerated apprenticeship. The people want a doctor who knows his job—who can, for example, recognise scabies when he sees it and tell them how to treat it. They are not particularly concerned whether he can discourse on Scabies in Mediæval Times or The Adaptive Mutations from which Evolved the Behaviour Pattern of *Acarus scabici*.

Would it be wrong to suspect that given freedom from G.M.C. recommendations a "model" curriculum would emanate from the Royal College of Physicians, which might even be prepared to send its representatives to the various medical schools to initiate the new era?

Department of Anatomy,
University of Glasgow. GEORGE M. WYBURN.

SIR,—The very interesting report by the Royal College of Physicians, prompts me to ventilate an idea which might possibly be applicable as an experiment at one, say, of our "red brick" universities.

It is, in effect, the introduction of a tutorial system, whereby each of the younger clinicians attached to the medical school would act as tutor to some five or six students for the whole of their undergraduate life. They would meet him perhaps for two one-hour sessions each week, on one occasion to discuss an essay he had set, and on the other for a general round-table conference. The value to the students would be obvious in bringing them from the first into personal contact with an active practitioner of their craft and would give them an initiation, particularly when they reached their clinical years, to the real as distinct from the textbook problems of medical work. The value to the tutor would hardly be less, since it would necessarily keep him up to date not only with other branches besides his own specialty but with his anatomical, physiological, and psychological knowledge.

One of the dangers of the age of specialism is that, while knowledge in a particular field may become ever more detailed and exact, the specialist is liable to fall behind even the newly qualified graduate where the rest of the subject is concerned; and my scheme would very effectively prevent this, since it would be useless to try and talk to a critical audience without an adequate familiarity with the matters under discussion.

Darlington. JOSEPH V. WALKER
Medical Officer of Health.

ECZEMA VACCINATUM

SIR,—I discussed the pathogenesis of Kaposi's varicelliform eruption in a paper [1] which described the virological investigation of 9 cases, including 3 of those reported by Sommerville and his colleagues [2] which were referred to by Dr. Napier (Jan. 14) in comment on the paper by Dr. de Salles-Gomes and his colleagues (Dec. 17).

Since then I have isolated herpes simplex virus from another 16 cases, including children involved in two outbreaks in dermatological wards, but have not encountered another case of eczema vaccinatum. In my experience, in mild cases the eruption may remain confined to areas of skin which *have been* affected by eczema, though it may spread beyond the boundaries of dermatitis active at the time. The disease may develop on a basis of unbroken skin in a phase of remission of eczema [1 3]—an observation which supports the hæmatogenous as against the surface-contamination theory of pathogenesis. Although secondary enlargement is to be expected in lymph-glands draining areas of skin affected by the pustular eruption, another point in favour of the hæmatogenous theory is that adenopathy may not only precede the appearance of the rash but may even be the presenting feature.[2 4] The general pattern of the classical case with its incubation period and sudden onset of febrile illness before the development of the eruption resembles that of other virus exanthemata in which viræmia is recognised as an essential stage.

Virus Laboratory, Ruchill Hospital, Glasgow, N.W. N. R. GRIST.

A NEW WAY OF TREATING FLAT FEET IN CHILDREN

SIR,—Mr. Sayle-Creer has long been an authority on this subject and consequently I read his letter (April 7) with interest and great care—perhaps more carefully than he read my article (Feb. 11). For though we agree in broad principle and in objective, it is a personal preference that condemns my conception of "flat feet," and there is no foundation for his claim that the device of Mr. Charlesworth [5] is similar to my heelseat.

He finds with me, though he states the case differently, that if the forefoot is left prone one can correct flat foot by inverting the heel. Mr. Charlesworth effects this by an admirable heel and arch support which extends to the heads of the metatarsals. It is an effective appliance, but to me it has the disadvantage of all arch supports in that it takes weight under the longitudinal arch. The original virtue of the *heelseat* is that it produces an arch while the foot bears weight only on the normal three points—viz., the heel and the heads of the first and fifth metatarsals. In this way the child's foot is allowed to develop normally, and once the arch is formed the foot is strong. Moreover it is important that the floor of the heelseat should not be wedged, for it is the weight of the child on the level surface which keeps the walls of the heelseat vertical and therefore maintains the position of the heel. If the base is wedged the heel slides to the outer side and produces the problem that Mr. Charlesworth discusses.

Mr. Sayle-Creer has quite reasonably given himself the prerogative of limiting the definition of "flat foot" to the foot with a flattened longitudinal arch. To all other flat feet in children he refers as pronated, everted, or valgus feet. With many other orthopædic surgeons, I am content to say that the feet are flat in any child that walks on the inner borders of the feet—whether the condition is due to a congenitally flat longitudinal arch or acquired by "everting the heel of an otherwise normal mobile foot." The difference is one of terminology only, and perhaps for the purpose of the article, which is to describe a method of treatment, Mr. Sayle-Creer will permit both types to be called flat feet—for if he will try the heelseat with persistence he will find that even the congenital flat foot can so be treated.

Judging by the number of queries that I have had from many parts of the world, I am happy and relieved to find that the "heelseat" seems to be regarded as both original and useful by orthopædic surgeons, pædiatricians, and specialists in physical medicine.

Newlands, Cape, South Africa. ARTHUR J. HELFET.

1. Grist, N. R. *Glasg. med. J.* 1953, **34**, 1.
2. Sommerville, J., Napier, W., Dick, A. *Brit. J. Derm.* 1951, **63**, 203.
3. Snyder, W. *Arch. Derm. Syph., Chicago*, 1951, **64**, 789.
4. McLachlan, A. D., Gillespie, M. *Brit. J. Derm.* 1936, **48**, 337.
5. Charlesworth, F. Chiropodial Orthopædics. Edinburgh, 1951.

MYASTHENIA GRAVIS

SIR,—Your editorial last week reveals a remarkable failure to understand the significance of recent investigations into the defect of neuromuscular transmission in this disorder. Thus, you state that the conclusions we drew from the response of myasthenics to the administration of decamethonium are opposed to those of Grob et al.,[1] which are based on the effect of the intra-arterial injection of acetylcholine. It is with the intention of correcting the confusion of thought that must have been created that we should like to re-state the generally accepted interpretation of these results.

Decamethonium (C10) has been shown to act at the myoneural junction in a similar manner to acetylcholine [2] but with the difference that because it is not rapidly destroyed by cholinesterase its actions can be readily studied. Using this drug in cases of myasthenia we demonstrated [3] that, whereas in normal subjects it acted as a pure depolariser, in myasthenics it acted by a fleeting depolarisation followed by a more prolonged non-depolarisation (i.e., curare-like) block—the so-called dual response. The fact that in myasthenics, as in normal subjects, decamethonium can be recovered unchanged from the urine indicated that the abnormal response to decamethonium was a property of the motor end-plate. On the basis of these results we put forward at that time the theory that the underlying mechanism at fault in myasthenia was an alteration in the manner in which the motor end-plate responded to acetylcholine or one of its breakdown products.

In 1955 Grob and his colleagues reported the results of their work using the intra-arterial injection of acetylcholine. In essence, they found that the response in both normal and myasthenic subjects was in two phases: first, a prompt depression of muscle activity (depolarisation block) which lasted about a minute and was soon followed by a secondary depression which persisted for thirty to sixty minutes. This late depression was found to be identical with the effect of the injection of choline—a breakdown product of acetylcholine. Furthermore, they noted that, whereas acetylcholine produced a rapid depolarisation block in both normal and myasthenic patients, choline gave rise to a depolarisation block in normal subjects and a non-depolarisation block in myasthenics. In other words, the injection of acetylcholine in myasthenic subjects gives rise to a "dual block"—i.e., a fleeting depolarisation block (due to acetylcholine) followed by a prolonged non-depolarisation block (due to choline). On the basis of their results these authors were unable to say "whether this abnormal response was due to a change in the myasthenic end-plate itself, or to the formation in myasthenic patients of a product of choline which is a competitive blocking agent." However, after comparing our results with their own they conclude: "this suggests that the myasthenic end-plate may react abnormally . . ."

1. Grob, D., Johns, R. J., Harvey, A. M. *Amer. J. Med.* 1955, **19**, 684.
2. Burns, B. D., Paton, W. D. M. *J. Physiol.* 1951, **115**, 41.
3. Churchill-Davidson, H. C., Richardson, A. T. *Ibid*, 1953, **122**, 252.

It is obvious, therefore, that both our results are in the closest possible accord and that together they supply convincing evidence that the abnormality in myasthenia is an alteration in the response of the motor end-plate to acetylcholine.

St. Thomas's Hospital, London, S.E.1. H. C. CHURCHILL-DAVIDSON
Royal Free Hospital, London, W.C.1. A. T. RICHARDSON.

PARATYPHOID-C OSTEOMYELITIS

SIR,—In their article of April 7 Dr. White and Dr. Meynell review the reported cases of osteomyelitis due to salmonella and indicate the rarity of this condition, particularly in salmonella infections other than *Salmonella typhi* and *Salm. paratyphi B*. The following recent case of osteomyelitis of the parietal bone due to *Salm. dublin* may therefore be of interest.

A woman, aged 72, was admitted to hospital, under the care of Dr. C. W. Walker, with severe anæmia. On examination she was confused and had early heart-failure and right basal pneumonia. A swelling was present over the left parietal bone. A blood-count showed Hb 37%, packed-cell volume 20%, mean corpuscular hæmoglobin concentration 27·5%, and white cells 10,000 per c.mm., with a pronounced shift to the left. Radiographs of the skull suggested a vascular tumour in the parietal bone. The presumptive diagnosis of secondary carcinomatosis from an unknown primary was made. The patient's condition initially improved with blood-transfusion and penicillin. Her condition then gradually deteriorated and she died on March 23. On retrospective inquiry it was discovered that the patient had had mild diarrhœa in the hospital.

At necropsy the parietal bone was found to be eroded and there was a collection of pus in the adjacent subaponeurotic and epidural spaces, cultures of which yielded a profuse growth of *Escherichia coli*, *Clostridium welchii*, and *Salm. dublin*. *Salm. dublin* was also found in cultures from the intestine.

On histological examination the parietal bone showed chronic granulomatous osteomyelitis with a predominance of mononuclear phagocytes, as in a typhoid lesion. Similar granulomatous lesions were present elsewhere in the body. Sections of the sternum, however, showed infiltration with carcinoma cells.

On later inquiry it was learnt that the patient had lived on a smallholding where losses from calf diarrhœa—a condition frequently associated with *Salm. dublin* infection—had been a feature.

It seems probable that the course of this patient's infection with *Salm. dublin*—an organism which only rarely causes a systemic infection in man—was influenced by a lowered state of resistance due to the concurrent carcinoma.

MARGARET E. BARTON
D. R. CHRISTIE
County Hospital, Hereford. K. VALTERIS.

ANTENATAL DETECTION OF HEREDITARY DISORDERS

SIR,—The recent articles on a technique for determining the ABO blood-group from epithelial cells [1] and confirmation [2] of the recognition of sex from epithelial cells from the amniotic fluid [3] have opened up the possibility of a new field of preventive medicine.

It should eventually be possible for most prospective parents with inherited disorders transmitted by single genes to obtain a fairly precise estimate of the likelihood of their coming child being affected by the twelfth week of pregnancy,[3 4] when termination would be simple and would not impair subsequent fertility. About half such pregnancies would be affected, and their interruption would probably not reduce the number of live births finally achieved by most parents. At present such terminations would be illegal, except possibly in incipient erythroblastosis fœtalis.

In sex-linked recessive disorders, such as hæmophilia, the interruption of girl-bearing pregnancies would eliminate transmission through known cases.

The reduction in the transmission-rate of disorders determined by autosomal dominant genes requires knowledge of their linkage with genes determining the observable behaviour of the amniotic cells. One such linkage with the ABO system has recently been described.[5] The development of methods of recognising genetically determined attributes of such cells, and an increased knowledge of linkage in man, should enable a great reduction to be achieved in the transmission of such diseases as Huntington's chorea, polyposis coli, arachnodactyly, and acholuric jaundice, without acting against the desires of the majority of afflicted persons.

The prospect of such preventive measures, and of relevant legislation, is particularly important in that not only are environmental improvements allowing increased proportions of afflicted infants to mature, but the increasing exposure to X rays, atomic piles, and experimental war will inevitably increase the mutation-rate in man.

London, N.1. J. H. EDWARDS.

PERFORATED ACUTE AND CHRONIC PEPTIC ULCER

SIR,—I would like to support Mr. Hermon Taylor and Mr. Warren (April 14) in their opinion that not all perforated peptic ulcers should be treated in the same way, and agree with their treatment policy as far as it goes, having arrived at the same conclusions for other reasons.[6]

I say "as far as it goes," for no less than 7 patients out of 93 were considered to be moribund on admission and their deaths inevitable; no details are given of these patients. As I pointed out in my paper, patients who are gravely ill from the peritoneal effects of a perforated ulcer will all die if treated by aspiration, but some will recover if the peritoneum is cleared of free fluid at operation and vigorous resuscitation is applied, and reinforced by noradrenaline if there is no response to the usual methods.

Exeter. H. DENDY MOORE.

RECURRENT DISLOCATION OF THE SHOULDER

SIR,—I might have overlooked the specious simplicity of your leader (April 14) had it not cast a reflection on the activities of that hard-worked branch of the profession—the orthopædic surgeon, imputing to him slackness in investigating an apparently simple problem.

The fact to be decided is whether or not immobilisation after a recent dislocation of the shoulder is a contributory factor to the development of recurrent dislocation. As you say, no protagonist of either side really knows, but to add "one of them must be wrong" is carrying logical positivism too far. It is highly probable that one group of shoulder dislocations, possibly those associated with a deep depression on the head, always recur regardless of the treatment, and another group, without bone injury, show a reduced recurrence-rate after adequate immobilisation. In fact very considerable attention has been given to this problem, and the failure to solve it suggests that there must be some overlapping of the effects of immobilisation and non-immobilisation, and is strong evidence that both sides might be right!

The leader goes on to state that "A definite answer could be given by a follow-up study of a few hundred cases treated by each method." This is an over-simplification. The fact is, that we have not even got an accurate figure for the recurrence-rate in a hundred cases treated

1. Coombs, R. R. A., Bedford, D., Rouillard, L. M. *Lancet*, April 21, 1956, p. 461.
2. Dewhurst, C. J. *Ibid*, p. 471.
3. Sachs, L., Steer, D. M., Danon, M. *Science*, 1956, **123**, 548.
4. Alvarez, M., Caldeyro, R. *Surg. Gynec. Obstet.* 1950, **91**, 1.
5. Renwick, J. H., Lawler, S. D. *Ann. hum. Gen.* 1954, **19**, 312.
6. *Lancet*, 1955, **i**, 163.

by any method, due to the difficulties of following up a series of cases in a moving population, and determining the frequency of complications which may arise many years after the original injury. Further, the disease is primarily a disease of the active years of life and does not occur in children or in the elderly, with the sole exception of epileptics. It is, therefore, not so easy to collect even in a busy clinic an adequate number of cases, for an essential part of the investigation must be a study of the mode of treatment employed in the reduction of the dislocation. This you do not mention.

It is quite probable that in the past Kocher's manœuvre as carried out under insufficient anæsthesia contributed a considerable quota of cases. Since the use of thiopentone and modern relaxants, the ease with which a shoulder can be reduced has been so increased that no additional capsular damage need be done in the majority of cases, and it is my impression that the frequency of recurrence is slowly declining.

Even if one could collect a group of cases in the appropriate age-group reduced by the same method and treated by alternate fixation and immobilisation, one's conscience might trouble one, as one cannot suggest a method of investigation which would not impose a hardship on the patient. Even if the recurrence-rate were as high as one in ten, an individual, faced with the choice of three weeks' immobilisation to avoid that risk and the certainty that if a recurrence did occur a straightforward operation followed by three weeks' immobilisation and perhaps a further three weeks' rehabilitation would cure it, would prefer to take his chances of having to be immobilised later rather than immediately.

I have tried to make some comparisons between the methods in the past and have been defeated by the almost instinctive resistance of the patient who when he feels his shoulder is right will take it out of his sling and use it regardless of the advice given to him. In my experience one of the surest ways of losing a young patient from the clinic is to immobilise him for three weeks after a dislocation. Only a few of the more phlegmatic patients will continue under this régime without raising question.

This is an interesting clinical problem but it appears it will only be solved by central registration of dislocated shoulders, uniformly treated, and a further registration of their recurrence. When the answer would appear to warrant this, I have no doubt somebody will find the necessary energy to answer your questions.

London, W.1. J. G. BONNIN.

BREAST CHANGES IN FIBROCYSTIC DISEASE OF THE PANCREAS

SIR,—Dr. Stroud and Dr. Heppleston, in their letter last week, illustrate the changes in the breast of a 6-week-old child, and conclude that the enlargement was due to "mastitis neonatorum." With this conclusion I entirely agree (though I dislike the term), and there is no need to invoke "mucoviscidosis" or antibiotic therapy.

I have examined histologically the breasts of many infants aged 0–6 months, and in a series of 115 such infants the histological picture illustrated by Stroud and Heppleston was found 15 times. This series was collected in the immediate post-war period, when the only antibiotic in general use was penicillin. This particular histological picture was not the only one responsible for enlargement, although the largest breasts usually showed this appearance. A secretory picture similar to that of the lactating adult breast is also common, and may produce quite considerable enlargement. The cystic change illustrated by Stroud and Heppleston may be a stage in the normal progression from the secretory to the resting (prepubertal) phase, since it was found to have a maximal incidence about the 2nd–3rd week, while the secretory picture was found maximally in the first 7 days of life. The prepubertal picture does not appear until the 4th week onwards. The oldest case showing the cystic appearance was 18 weeks. Pictures intermediate between secretory and cystic, and between cystic and prepubertal, were found in 14 of the 115 cases.

I have no details of antibiotic therapy in these cases, but there appeared to be no correlation with any particular disease process, and the sex-distribution was equal—8 boys and 7 girls.

Department of Pathology,
Bedford General Hospital. J. C. VALENTINE.

*** Through a misunderstanding of ours it was stated in the letter by Dr. Stroud and Dr. Heppleston that case 1 was one of Dr. Jolly's three cases (*Lancet*, 1955, ii, 1136). In fact cases 1 and 2 were seen in the department of child health of the Welsh National School of Medicine.—ED. L.

FLUIDS FOR INTRAVENOUS INFUSION

SIR,—For some years I have used a brand of vacuum-bottled sterile intravenous-infusion fluids and have felt able to rely on these products. Within six months I have found a faulty vacuum in four bottles (isotonic saline three, isotonic-saline/glucose one) and in one of each the pressure was a little above atmospheric. Apparently complaints of this kind are rare: I have heard of no similar experiences. Every bottle that I use I open myself, and I wonder if such faults are missed when nurses open bottles and either do not appreciate or do not report the defect.

The method of bottling used by this firm makes it hard to see how the vacuum can fail, and no-one so far has given a satisfactory explanation of the origin of a pressure above atmospheric (around 10 cm. of water in one case). I would urge anæsthetists and others setting up "drips" to watch for a lack of bubbling (or for frank squirting out of the solution) when the caps are removed from such bottles, and not merely to discard them but to report such events to the makers.

London, E.11. JOHN BARNARD.

HÆMATEMESIS

SIR,—I feel that Dr. Bancroft's comments (April 14) on my article (April 7) are reasonable and should be answered.

The method was used, in the first instance, only on the very late case of hæmatemesis—the case that almost invariably ended fatally. It was used, therefore, as an alternative to emergency gastrectomy and was found to give better results. The only remaining procedure for obtaining direct controls would have been to retain 50% of these patients on a régime which had already failed.

The most positive proof I can offer is the way in which patients who have failed to respond to routine medical treatment cease bleeding after the administration of adrenaline and 'Stypven.' This statement can be confirmed or discredited only by an actual trial of the method. We found at an early stage in the investigation that gastric lavage and stypven in doses of up to 20 ml. were often ineffective, yet when repeated in conjunction with adrenaline the bleeding was immediately controlled—though, as I discovered subsequently, only temporarily in a proportion of cases of true "surgical" hæmatemesis.

The main point at issue for the physician and surgeon alike is to recognise "surgical" hæmatemesis early. As a rule patients are transferred to a surgical ward for one of two reasons: either because they comply with the standard criteria for surgery, or because they will not respond to medical treatment after the most patient and persistent endeavour. In the first instance we observed a 30% error in diagnosis, and in the second the results of operation were not encouraging.

The sole purpose of the procedure is to help in the early selection of the case that must be treated by surgery. The method is so simple and safe that I can see only two valid objections to its use: one medical and one surgical. The dosage of adrenaline employed is unlikely to receive ready acceptance by one who has been trained to use it in carefully calibrated doses of up to as much as 1 ml. or by the young surgeon who must depend on emergency operations for his quota of gastric surgery.

"Men occasionally stumble over the truth but most of them pick themselves up and hurry off as if nothing had happened" (Sir Winston Churchill).

Carnwath, Lanarkhire. W. J. M. BRANDON.

PREVENTION OF RENAL LESIONS DUE TO ISCHÆMIA

SIR,—In view of the interest aroused by "artificial hibernation" we wish to draw attention to the effect of this procedure on ischæmic lesions of the kidney.

Renal ischæmia constitutes a major problem in operations for partial nephrectomy and in shock.

Partial nephrectomy necessitates temporary compression of renal vessels. No untoward consequences result from this if the other kidney is normal, since function is restored within a few weeks, even after circulation has been arrested for a whole hour. On the other hand if the patient has only one kidney and this must be operated on, ischæmia of ten minutes' duration may be tolerated, but the safety margin is dangerously narrow and the outcome depends mainly on the duration of ischæmia.[1]

In *shock*, whether due to injury, loss of blood, or any other factor, one of the chief complications is a renal lesion, which has caused the death of many a patient whose circulatory equilibrium had successfully been restored.[2] The lesion, whether directly or indirectly, is always the consequence of ischæmia. The tubular system is injured by anoxia; simultaneously with the decrease of circulation there is a decrease in glomerular filtration, and, in consequence of anuria, in the tubules casts are formed and toxic effects manifest themselves.[2 3]

In animals, clamping the renal artery for four hours, three to four weeks after the other kidney has been removed, usually leads to death in uræmia. Compression for two hours is usually survived, although complete restoration of renal function takes two to three weeks.[4–6]

The pathogenesis of uræmia following renal ischæmia is identical with that associated with shock, and the morphological changes are also the same.[5 7] Considering that in both forms the basic problem is the disproportion between oxygen need and oxygen supply, it was assumed that by decreasing the tissues' oxygen demand it should be possible to prevent injury by ischæmia. Experiments were therefore carried out to study the development of the lesions in hypothermia after administration of chlorpromazine.

12 dogs which had had their right kidney removed three weeks before were used in the experiments. They were divided into two groups. In the control group of 6 animals, the renal artery was clamped for four hours at normal body-temperature. In the "hibernated" group first 5 mg. of chlorpromazine per kg. body-weight was administered in an intravenous infusion in two hours. Then the animals were cooled to 24–25°C, and the renal artery was laid bare and compressed by means of a surgical clamp, with care to avoid crushing the accompanying nerves. After four hours the clamp was released and the animals were re-warmed. Before arresting renal circulation, two normal clearance periods had been registered and also the non-protein-nitrogen level in the plasma. After releasing the artery it was checked whether circulation had become normal in the kidney. For fourteen days plasma non-protein-nitrogen values, and *p*-aminohippurate and creatinine clearances, were determined every day in each animal. The survivors were killed on the fourteenth day.

Of the 6 animals in the control group, 5 died of uræmia within nine days. Their plasma non-protein-nitrogen level ranged from 156 mg. to 297 mg. per 100 ml. from the fourth day onwards. Uræmia had also developed in the 6th dog, but this subsided by the fourteenth day. In the hypothermic group all 6 animals survived. In 5 animals the non-protein-nitrogen level did not rise above the upper limit of normal (26–49 mg. per 100 ml.); in 1 there were high values for a few days.

In the control group, grave cortical necrosis was present in every kidney, with calcium deposits in the tubules, extensive œdema, epithelial necrosis, and masses of casts, and, in addition, cellular infiltration from the renal pelvis. In the hypothermic group, renal lesions were very slight, not exceeding some hydropic degeneration of a few tubules.

In the control group, by the fourth day the clearance of *p*-aminohippurate had decreased, on average, to 26% of the initial value; that of creatinine, to 16% (in agreement with the findings of others[8 9]). In the hibernated group, *p*-aminohippurate clearance remained normal in 4 dogs, while in the other 2 it decreased temporarily but regained the initial value before the fourteenth day. Creatinine clearance did not change in 3 dogs; in 3 it decreased by 20–29%, and in 2 of these it was normal before the fourteenth day.

We conclude from these observations that the lethal kidney lesion which develops as a result of ischæmia can practically be prevented by administration of chlorpromazine and subsequent cooling. Since in previous experiments[10] it was found that the changes in renal function occurring in hypothermia do not persist after body-temperature has been raised to normal, on the basis of the present findings we feel justified in recommending administration of chlorpromazine and subsequent hypothermia preoperatively for operations in the course of which renal circulation is arrested. Moreover, it seems probable that this procedure may help to prevent the renal lesions associated with shock.

The findings described here are to appear in full in *Acta Physiologica Hungarica*.

P. V. VÉGHELYI
1st Department of Pædiatrics and Institute of Physiology, L. HÁRSING
Budapest University Medical School. K. LÁSZLÓ.

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Appointments

BERESFORD, C. C., M.B. Lond., D.P.M.: physician-superintendent, The Retreat, York.

BLACK, DAVID, M.B. Belf., D.O.M.S.: part-time asst. ophthalmologist, Walton Hospital, Liverpool.

CHURCHILL-DAVIDSON, I. F. J., M.B. Camb., D.M.R.T.: physician, radiotherapy department, St. Thomas's Hospital, London.

GARAI, O. F., M.R.C.P.: part-time clinical asst., cardiographic department, Charing Cross Hospital, London.

JEFFERSON, K. E., M.B. Camb., M.R.C.P., F.F.R.: part-time consultant radiologist, Brompton Hospital, London.

NICOL, C. S., M.D. Lond., M.R.C.P.: physician, department of venereal diseases, St. Thomas's Hospital, London.

Births, Marriages, and Deaths

BIRTHS

OSTLERE.—On April 19, at King's College Hospital, S.E.5, to Mary (née Patten) and Gordon Ostlere—a son.

DEATHS

MORRISH.—On April 14, at Stafford, William John Morrish, M.D. Lond., M.R.C.P., D.P.H., late of Streatham Park, London, S.W.16.

Obituary

ARTHUR HUGH McCULLOCH EATON

M.B. Belf., F.R.C.S.E.

Mr. Eaton, senior surgeon to the Tyrone County Hospital, died on April 1. The youngest son of the late Mr. and Mrs. J. C. Eaton, Altnagelvin, Derry, he was educated at Foyle College and Queen's University, Belfast. He served in the 1914–18 war as a surgeon probationer in the R.N.V.R., and on demobilisation he returned to Queen's and graduated with honours in 1922. After taking the F.R.C.S.E. in 1927, he was appointed as surgeon in the Tyrone County Hospital, Omagh. As a Territorial officer he was called up in 1939 and he served in Boulogne until the evacuation in 1940. At the request of the Tyrone hospital committee he was recalled to his civilian post before the end of the war. He served as president of the Northern Ireland branch of the British Medical Association, of the Omagh branch of the British Legion, of the Tyrone branch of the British Red Cross Society, and of the Tyrone County Club. He was also a member of the Tyrone Grand Jury.

W. S. B. writes: "Mr. Eaton was one of the small band of surgeons working in country hospitals in Ulster who bore the brunt of surgery for so many years until the introduction of the health service. The fact that his hospital, from small beginnings, became one of the largest Ulster hospitals outside Belfast was due to his continued efforts, administrative skill, and personality, as well as his surgical skill. He was a quiet and unassuming man who, despite the early age at which he took up his appointment, foresaw the possibilities of development in country-hospital work. Such were his sound common sense and the confidence that he inspired in his hospital committees that he was able to build up outpatient-clinic organisations and form a nucleus of a fuller medical staff, so that when the consultant and specialist services were introduced at the beginning of the health scheme his hospital was already well developed and able to take a full part from the beginning in the new era. In a provincial hospital the tie between staff, patients, and local people is, in many ways, stronger than in any of the larger city institutions, and Mr. Eaton will be sincerely missed, not only as their medical adviser but as their friend, by the great numbers of people who had benefited from his ceaseless hard work and kindly advice."

He leaves a widow and two daughters.

ALEXANDER GIBSON

M.A., M.B. Edin., F.R.C.S.E.

Dr. Gibson, consulting orthopædic surgeon to the Winnipeg General Hospital, whose death at the age of 73 has been announced, was one of the many distinguished emigrants whom Scotland has sent to Canada.

He was born in Edinburgh and educated at the university there, graduating M.B. with first-class honours in 1908, and winning the Vans Dunlop and Ettles scholarships. He held a university demonstratorship in anatomy before he came to London to continue his surgical and anatomical studies. After taking the F.R.C.S. in 1913 he was appointed to the chair of anatomy in the University of Manitoba. During the first world war he served with the Canadian Forces in India and Egypt, and during the late war he was in charge of a Canadian Red Cross unit in Scotland. He was a past president of the Canadian Orthopædic Association and surgeon in charge of orthopædics at Winnipeg Military Hospital.

An English colleague who had met him at meetings in London and Quebec writes:

"For many years Alexander Gibson's name has been familiar to orthopædic surgeons in this country from his publications, particularly in connection with the surgery of the hip-joint, though for many of the younger generation the first chance of the pleasure of his personal acquaintance came on his visit to Britain in 1952 for the Orthopædic Meeting of the English-speaking World—and it was a real pleasure. He had the gift of friendship. His writings were lucid and he was a most admirable speaker, forceful and clear in the best Scottish tradition. With our colleagues in Canada we share a sense of deep loss of a fine surgeon and a fine man."

Diary of the Week

APRIL 29 TO MAY 5

Monday, 30th

MANCHESTER MEDICAL SOCIETY
4.30 P.M. (Medical School, Manchester University.) Prof. A. Stampar (Zagreb): Public Health in Underdeveloped Countries.

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
4 P.M. Dr. Ian Gilliland: Exophthalmos.

Tuesday, 1st

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S.W.1
5 P.M. Dr. A. H. Douthwaite: Pitfalls in Medicine. (First of two Croonian lectures.)

UNIVERSITY OF LONDON
5.30 P.M. (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.) Prof. L. Kreyberg (Oslo): Ætiology and Occurrence of Lung Cancer in the light of Pathological Anatomy.

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
8.30 P.M. *Orthopædics.* Sir Reginald Watson-Jones: Treatment of Bone and Joint Injuries—past, present, and future. (Presidential address.)

INSTITUTE OF CHILD HEALTH
5 P.M. (Hospital for Sick Children, Great Ormond Street, W.C.1.) Dr. J. H. Ebbs (Toronto): Changes in the Stature of School-children in the last Half Century.

Wednesday, 2nd

UNIVERSITY OF LONDON
5 P.M. (St. Thomas's Hospital Medical School, S.E.1.) Dr. S. W. Kuffler (Johns Hopkins Hospital): Patterns of Innervation and Contraction in Striated Muscle.

ROYAL SOCIETY OF MEDICINE
4.30 P.M. *Proctology.* Dr. Neil Swinton, Mr. Bryan Brooke, Mr. Stanley Aylett: Ileostomy.
5.15 P.M. *History of Medicine.* Dr. Douglas Guthrie: The Hippocratic Oath.

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Dr. Henry Haber: Clefts, Vesicles, and Bullæ.

INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Dr. Paul Wood: Physiological Classification of Pulmonary Hypertension.

MANCHESTER MEDICAL SOCIETY
4.15 P.M. Dr. T. F. Fox: The Medical Empire.

MEDICO-CHIRURGICAL SOCIETY OF EDINBURGH
8.30 P.M. (Royal College of Surgeons, 18, Nicolson Street, Edinburgh.) Dr. I. W. B. Grant: Chronic Bronchitis.

Thursday, 3rd

ROYAL COLLEGE OF PHYSICIANS OF LONDON
5 P.M. Dr. Douthwaite: Pitfalls in Medicine. (Second of two Croonian lectures.)

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
11.30 A.M. Dr. H. C. Andersen (Denmark): Diagnosis and Screening of Deaf Children in Denmark.
12.15 P.M. Dr. Ole Bentzen (Denmark): Auditory Training in Denmark.

ST. JOHN'S HOSPITAL DERMATOLOGICAL SOCIETY, 5, Lisle Street, W.C.2
5 P.M. Prof. W. Montagna (Rhode Island): Reappraisal of the Phenomenon of Hair Growth.

HONYMAN GILLESPIE LECTURE
5 P.M. (University New Buildings, Teviot Place, Edinburgh.) Dr. J. H. Ebbs: Medical Services in the Canadian Arctic.

UNIVERSITY OF ST. ANDREWS
5 P.M. (Queen's College, Small's Wynd, Dundee.) Dr. A. A. Douglas: Birth Injuries of the Eye with particular reference to Congenital Squint.

Friday, 4th

UNIVERSITY OF LONDON
5 P.M. (St. Bartholomew's Hospital Medical College, E.C.1.) Prof. F. A. Simeone (Western Reserve University): Post-denervation Supersensitivity.

ROYAL SOCIETY OF MEDICINE
10.30 A.M. *Otology.* Dr. Hans Engström (Sweden): The Organs of Corti. Dr. Jan Wersäll (Sweden): The Structure of the Vestibular Sensory Apparatus.
2.30 P.M. *Laryngology.* Mr. K. Harrison, Dr. Helen Russell: Ectopic Salivary Adenomata. Mr. F. C. W. Capps, Prof. George Cunningham: Four Cases of Identical Tumour Associated with the Infra-orbital Nerve and its Sheath.
5.30 P.M. *Anæsthetics.* Dr. Robert Virtue (Colorado): Dihydroxycorticosteroids of Blood during Anæsthesia and Surgery.

POSTGRADUATE MEDICAL SCHOOL OF LONDON
10 A.M. Dr. Edward Hamlin, jun. (Harvard University): Thyroid Biopsies.

ST. MARY'S HOSPITAL MEDICAL SCHOOL, Paddington, W.2
5 P.M. Mr. G. W. Williams: Uterine Abnormalities and their Clinical Significance.

A memorial service for the late Sir MORTON SMART is to be held at the Savoy Chapel, London, on Wednesday, May 2, at 11.45 A.M.

Notes and News

FORWARDS IN MANCHESTER

"As a first step towards improving medical education in our University," Manchester are making some small but important adjustments in their curriculum.[1] Revision had become demonstrably necessary because of the difficulty of arranging a time-table: classes clashed; students were doing clinical work in one subject while taking an examination in another; and no fewer than four examinations had to be taken in the last 18 months. The object of the new arrangements is to remove these faults, to reduce the content of the course, to free at least one long vacation, and to provide a period, at the end of the course, for general revision.

In the new curriculum the 2nd M.B. examination will be held 3 months earlier, and the introductory course preceding the clinical period will be discontinued in favour of a different type of instruction to students during their first medical and surgical appointments. The time spent in the ear, nose, and throat, eye, and skin departments will be reduced from 3 months to 6 weeks and the period at the skin hospital from a month to a fortnight. The gynæcological appointment will be postponed to the final year and will include revision in obstetrics and pædiatrics. Forensic medicine will have a terminal examination, and social and preventive medicine will (very properly) come into all four subjects of the final (obstetrics and gynæcology, pædiatrics, medicine, and surgery). These and other changes will mean that no big examination is held between March of the fourth year and June of the sixth.

Only those who have tried to alter a curriculum have a true conception of the difficulty of making even minor changes. We congratulate the Manchester school on their improvements and trust that time will prove them right in describing these as "a beginning."

HOSPITAL ADMINISTRATIVE STAFF

LAST year in discussing the recruitment of hospital administrators [2] we mentioned a suggestion that King Edward's Hospital Fund should organise appropriate training for these men and women. The need for such a plan was urged more lately in the Guillebaud report and by the Whitley Council for administrative and clerical staffs. The King's Fund [3] has already announced its willingness to help and now the Government has launched a scheme that will make use of the Fund's offer.

Trainees, who may be from inside or outside the hospital service, will be selected to fill training posts for a course of a maximum of three years. They will be given practical experience of all branches of administration with different hospital authorities, along with courses of instruction at the Hospital Administrative Staff College of the Fund or the University of Manchester. 16 posts are available for the first course, beginning in September. The starting salary for trainees will be £540 (plus a small addition in the London area) with an increase of £20 in the second and third years. Trainees already in the hospital service will retain their present salary if higher than this. Fees and other expenses during training will be met. Young people under 18 in the hospital service will be helped to continue their general education, and hospitals will be encouraged to institute on-the-job training schemes to give them experience of various types of work.

HEALTH IN INDUSTRY

THE London Transport Executive have published a detailed statistical analysis on sickness absence—"the absence from work accepted by the employer as attributable to sickness or injury"—among their employees.[4] The book is the first analysis of its kind, and it will provide a standard for all concerned with the study of health in various branches of industry.

Sickness-absence statistics are not synonymous with morbidity statistics. The records do not cover the episodes of sickness or injury which do not prevent the patient from following his employment, chronic ill health which compels the patient to give up work altogether, or the sickness and injury of persons who are not employed and therefore do not come under an employer's observation. They include, however, many short spells of absence which are not registered for National Insurance or friendly society purposes, because of the "waiting days" for benefit. The problem is thus a specialised one, not covered in statistical tables hitherto available. Its magnitude is reflected in a statement by the *Manchester Guardian* [5]: "About seven million claims for sickness benefit are made each year, and the number of short absences from work because of sickness for which no claims are made is believed to be another six million."

The data given in this book raise a number of questions of social and medical importance. An interesting finding, for example, is that sickness which lasts more than four days tends to be measured in whole weeks. Though this will need further elucidation, it seems that National Insurance regulations keep people away from work when they would otherwise be well enough to return. On the other hand, we all know that a few days' convalescence after an acute illness may prove of benefit in the long run. Another problem of great importance is the comparison between the periods of sickness absences of the under-45 and over-45. It would seem that, though long spells of absence, due to serious illness, are more common over the age of 45, short sickness absences are considerably commoner in the younger age-group.

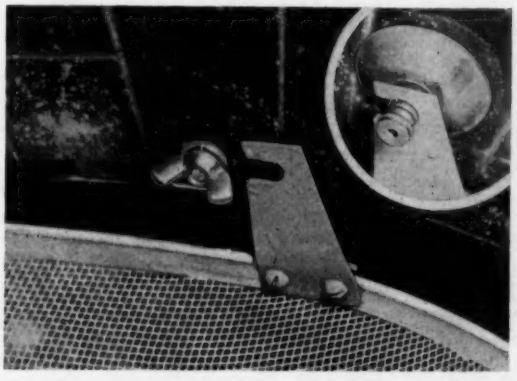
1. *Manchester University Medical School Gazette*, January, 1956, p. 11.
2. Lancet, 1955, ii, 78.
3. *Ibid*, p. 1331.
4. Health in Industry, Sickness Absence Statistics. London: Butterworths Medical Publications. 1956. Pp. 177. 35*s*.

SALARIES IN THE PUBLIC-HEALTH SERVICE

COMMITTEE C of the medical Whitley Council announces that agreement has been reached between the staff and management sides to recommend an increase in the salaries of doctors in the public-health service as from April 1, 1956. The increase will be of $7\frac{1}{2}\%$ on the first £1250 of salary and of 5% on the excess of salary over £1250.

IMPROVING A FIREGUARD

Dr. G. R. Hervey writes: Open fires still cause fatal accidents to children, in some instances even though a fireguard was in use. The type of guard which seems to be most commonly used today is good in that it has a closely woven wire mesh, but less good in being so light that it can easily be moved by a one-year-old. Fastening the guard to the fireplace overcomes this danger and greatly increases the safety given by the guard. The accompanying figure shows one way in



which this can be done, and the work required is well within the scope of any "handyman." The lugs are made from small pieces of sheet-metal. The studs in the wall are $1\frac{1}{2}$ in. × no. 14 woodscrews with the heads cut off and the straight part of the shanks threaded with $\frac{1}{4}$ in. Whitworth threads. Fixing them is easier than it looks. A hole is drilled through the tile and the cement beneath it with a no. 14 'Durium' drill; a no. 12 'Rawlplug' is inserted; and the stud is screwed in, held by two nuts temporarily screwed on to the shank and locked against each other. These are subsequently replaced by the wing-nuts and washers shown. If loosening or tightening the wing-nuts when the guard is moved is thought unduly burdensome, they can be replaced by domed washers backed by spring washers to give a friction grip. A further modification made to this particular guard was the addition of a piece of expanded metal at the top to close a gap which

5. April 13, 1956, p. 8.

would otherwise exist between the top of the fireplace and the top of the guard.

As an alternative to drilling holes in the fireplace, the studs can be mounted on rubber suction discs. The sucker shown in the accompanying inset figure was hardly good enough, but a better type which is used in a range of car accessories would give a very firm grip on a tiled fireplace. Perhaps some manufacturer of fireguards would consider this idea.

A BROCHURE FOR THE YOUNG PATIENT

FEW attempts are made to write intelligently on medical matters for young people of 12–16. Perhaps this is because they are a between-age group, neither child nor adult, for whom the English language does not even provide a generic name: "girl" is acceptable but "boy" barely so, and the two together fail to convey the right impression; "teenager" is American and in this country is applied generally to the 15 or 16 plus. We glance at them charily, and as subjects for medical literature pass them by with scarce a thought. They are not often seriously ill; they are seldom grouped together in a ward; and they have little opportunity of asking for information. Should we therefore ignore them? It has been the custom to do so, and custom is hard to change. A brochure designed especially to appeal to them pulls us up with a jerk.

The Brentwood Hospital Management Committee, with the help of the National Association for the Prevention of Tuberculosis, have produced such a brochure [1] for young patients who come to Highwood Hospital for treatment. While the result is not beyond criticism, the intention is unreservedly commendable; the effort to win the young patient's coöperation is a compliment that he will appreciate. The main objects of treatment are explained and the idea behind such treatment is conveyed—albeit rather haltingly. There is a tendency to talk down ("Be a good patient and do what the doctors and nurses tell you") which may arouse resentment; too much is in the abstract (as in the differentiation between "negative distractions" and "positive distractions"); and there is rather too much of the phraseology applicable to adult tuberculous patients ("tearing your nerves to pieces with worry," "imposing a kind of self-discipline," "you have to be a social and a human being"). But the basic idea is fundamentally right.

University of London

Dr. E. M. Glaser has been appointed to the readership in physiology at the London Hospital Medical College.

Dr. Glaser qualified from the University of Bratislava in 1938 and soon afterwards came to this country where he became a voluntary research assistant at the British Postgraduate Medical School. During his service with the R.A.M.C. in the late war he received the M.C. In 1949 he took the PH.D. Camb. and in 1951 the M.R.C.P. As a member of the Medical Research Council's scientific staff he worked in the department of experimental medicine at Cambridge. Since he took up his present post as King Edward professor of physiology in the University of Malaya he has continued to serve on the M.R.C.'s standing advisory committee on climatic physiology. His published work includes papers on the prevention of motion sickness.

Dr. J. C. Sloper has been appointed to the readership in morbid anatomy at Charing Cross Hospital Medical School.

Dr. Sloper received his medical education at Cambridge and the London Hospital. After qualifying in 1945 he held house-appointments at the London. He took the M.R.C.P. in 1946 and the M.D. Camb. in 1951. He is at present senior lecturer in morbid anatomy at the London. He has published papers on Addison's disease, mycotic infections, and idiopathic diffuse muscular hypertrophy of the œsophagus.

The title of professor of genetics has been conferred on Dr. Hans Grüneberg, F.R.S., in respect of his post at University College.

National University of Ireland

The degree of M.D. has been awarded to Edward O'Sullivan.

University of Dublin

On Thursday, May 10, at 5 P.M., at Trinity College, Dr. Moacyr E. Alvaro, president of the Pan American Congress of Ophthalmology, will deliver the Montgomery lecture, when his subject will be the Ætiology and Pathogeny of Uveitis. Prof. A. St.G. Huggett will give the John Mallet Purser lecture on Thursday, May 24, at 4.30 P.M., when he will speak on Environment of the Fœtus and Postnatal Health.

Royal Society of Medicine

The gold medal of this society has been awarded to Sir Gordon Gordon-Taylor.

1. How to Get Well Soon at Highwood Hospital. Published by Brentwood Group Hospital Management Committee.

Empire Rheumatism Council

On Tuesday, May 1, at 2.45 P.M. the annual general meeting of this council is to be held at St. James's Palace, London, when the Duke of Gloucester will preside.

Medical Association for the Prevention of War

This association is holding a conference at 90, Buckingham Palace Road, London, S.W.1, on Saturday, May 5, at 2.30 P.M., on the Development of the Child in the Cold War Era.

International College of Surgeons

This college has awarded its scholarship ($3000) to Mr. W. F. Walker, of Dundee, who is to spend a year with Professor Moore, of Boston, working on surgical metabolic problems.

Navy Medical Compassionate Fund

A meeting of the subscribers of this fund will be held at 2.30 P.M. on May 4 at the Medical Department of the Navy, Queen Anne's Mansions, St. James's Park, London, S.W.1, to elect six directors.

Royal Appointment

Surgeon Captain E. B. Pollard, R.N., has been appointed an honorary surgeon to the Queen in succession to Surgeon Captain J. V. Williams, R.N.

New Medical Director of Navy

As announced last October Surgeon Vice-Admiral R. C. May is to succeed Surgeon Vice-Admiral Sir Alexander Ingleby Mackenzie as medical director-general of the Navy. Sir Alexander retires on April 30.

Central Council for the Care of Cripples

The annual general meeting of this council will be held on Thursday, May 3, at 3 P.M., at County Hall, London, S.E.1, when Mr. Iain Macleod, the Minister of Labour and National Service, will speak.

Medical Exhibition

The organisers of the London Medical Exhibition are holding their regional exhibition this year in Cardiff from May 7 to 11.

Queen Charlotte's Maternity Hospital, London

On Thursday, May 3, at 2.15 P.M., a meeting will be held at this hospital, Goldhawk Road, W.6, to commemorate the 25th anniversay of the opening of the Bernhard Baron memorial research laboratories and the isolation block. Dr. Leonard Colebrook, F.R.S., and Mr. G. F. Gibberd will speak.

Chiropody for Old People

The National Corporation for the Care of Old People announce in their annual report for 1955 that they have set aside £60,000 to be spent over three years in making grants to voluntary organisations providing chiropody at reduced rates for needy old people.

Course on Personnel Administration

The Ministry of Health announces (H.M.[56]34) that the Royal College of Nursing has arranged a course on this subject from June 4 to 15. Hospital authorities, especially those concerned with the management of mental or mental-deficiency hospitals where staffing problems are acute, are asked to consider giving their matron or chief male nurse facilities to attend. The fee for the course (25 guineas) would, it is suggested, be "a suitable use for non-exchequer funds." Applications for membership should be made to the college, Henrietta Place, London, W.1.

Appeal for a Students' Summer School

The London region of the British Medical Students' Association is organising a national clinical summer school to be held in London from Sept. 2 to 16. This school will be attended by 50 students from all over the British Isles, and by 15 Yugoslavian students as part of a British-Yugoslavian exchange scheme. The students will pay their fares and £14 towards their accommodation; but further outlay will have to be met in arranging visits to hospitals and other institutions. The association also hopes to help the Yugoslavians with their heavy travelling expenses. Contributions should be sent to the hon. secretary of the association, B.M.A. House, Tavistock Square, London, W.C.1.

NEW approach in

SKIN DISEASE

Inflammation with Infection

DEMANDS
'HYDROCORTONE' AND ANTIBIOTICS

'HYDRODERM' provides the anti-inflammatory steroid hydrocortisone, incorporated in an emollient base with the antibiotics neomycin and bacitracin. Specific activity is provided against both inflammation and infection. Use of these two broad-spectrum antibiotics assures protection from a wide variety of organisms commonly found in skin lesions. Neither neomycin nor bacitracin is likely to cause a local reaction, and their use does not contra-indicate the concurrent use of other antibiotics systemically. Topical Ointment of 'HYDRODERM' is supplied in tubes of 5 G. and 15 G.

Indications

Atopic dermatoses	Contact dermatoses
Allergic eczema	Allergic reactions due to:
Infantile eczema	Drugs
Eczematoid dermatitis	Cosmetics
Food eczema	Chemicals
Pruritus with lichenification	Soaps
	Plants
	Clothing

Non-specific anogenital pruritus

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TOPICAL OINTMENT

(Hydrocortisone - Neomycin Sulphate - Zinc Bacitracin)

Literature and professional package available to physicians on request.

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Bavarian spas can help doctors to cure their patients

MANY of the health-resorts in Bavaria have been known for centuries past and are world-famous. Thousands of patients from all parts of the world recover their health in the fashionable climatic resorts, the spas and sanatoria in and arround the Bavarian Alps.

The greatest care is devoted to the patients' well-being. Local medical specialists work in close cooperation with their colleagues abroad for the benefit of their patients.

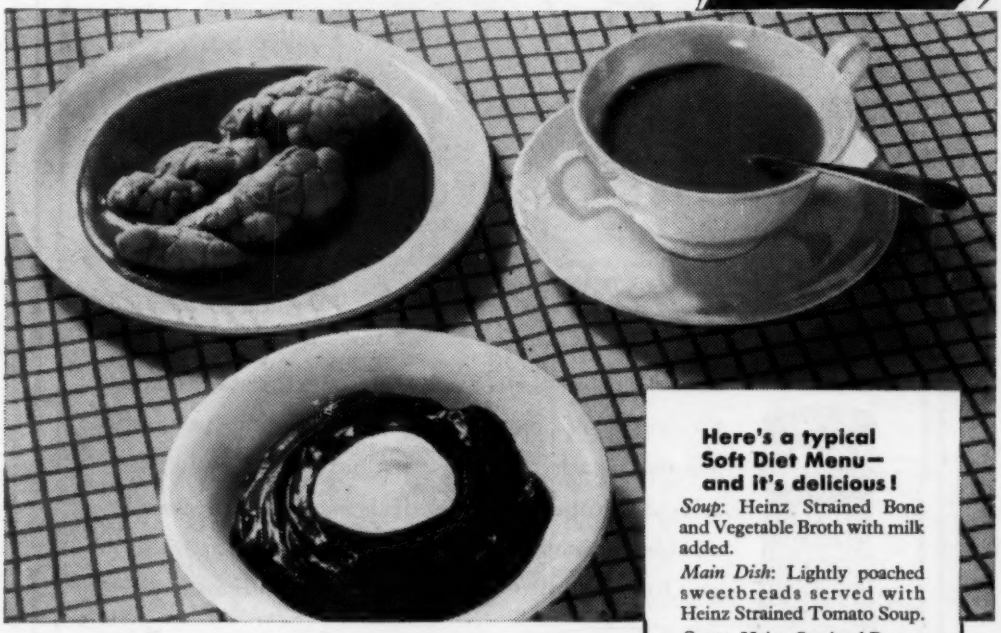
A detailed description of the 27 Bavarian health-resorts and spas will be sent on request.

TREATMENT OF:

Cardiac and vascular diseases • Muscular rheumatism • Rheumatism of the nerves and joints • Diseases of the respiratory organs • Diseases of women • Gastric, intestinal, hepatic and bilious complaints and metabolic disorders • Disorders of the hæmopoietic system • Neuralgia and neuritis • Endocrine disorders and those due to overstrain • Convalescence • ***Prospectuses available from the local spa Information Office (Kurverwaltung), and German Tourist Information Bureau, 6, Vigo Street, Regent Street, London, W.1.***

A copy (twenty pages) of "Cures in Bavarian Health Resorts" is available on application to Bayerischer Heilbaederverband, Bad Kissingen, West Germany.

"I don't think you'll mind this Soft Diet!"



You probably sympathise with the patient you put on a Soft Diet . . . he usually looks very glum as he imagines tedious gruels and unsatisfied hunger.

But his imaginings can be groundless. With Heinz Strained Foods a Soft Diet can be both satisfying and pleasant nowadays.

The wide range of Heinz Strained Foods provides all the variety your patient expects to miss. They contain no strong seasoning and all coarse fibres are removed.

Heinz Strained Foods are prepared and cooked by scientific methods to conserve maximum nutritive values, making them actually more nutritious than similar foods prepared at home.

For hospital use, Heinz Strained Foods are obtainable in 15½-oz. cans from the usual suppliers or direct from H. J. Heinz Company Ltd., Harlesden, N.W.10.

Here's a typical Soft Diet Menu—and it's delicious!

Soup: Heinz Strained Bone and Vegetable Broth with milk added.

Main Dish: Lightly poached sweetbreads served with Heinz Strained Tomato Soup.

Sweet: Heinz Strained Prunes with whipped cream.

HEINZ STRAINED FOODS

Beef Broth with Beef and Barley
Beef and Liver Soup
Bone and Vegetable Broth
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Tomato Soup · Vegetable Soup
Beetroot · Carrots · Peas
Green Beans · Creamed Spinach
Apple, Prune and Custard
Apples · Egg Custard with Rice
Plums with Semolina
Prunes with Cereal
Creamed Cereal
Chocolate Pudding
Apricots with Rice

57 HEINZ Strained Foods make a Soft Diet interesting

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Scott's Twin-Pack feeds, protects, soothes and educates. It feeds because each ounce gives over 100 calories. It protects and soothes because it is fortified by the addition of Vitamin D, calcium and trace elements, whilst it also contains Vitamin B_1 which is associated with the development of healthy nerve tissues. Moreover, Scott's Twin-Pack is easily digested and assimilated. Finally, Scott's Twin-Pack helps to educate baby's taste and pave the way towards a full varied diet, because each of the two cereals has its own distinct flavour.

Scott's Twin-Pack consists of pre-cooked and prepared oats and wheat, each in a separate waxed paper container, within the specially protected outer pack. It accords perfectly with modern teaching of the early addition of solids and variety to a baby's diet.

THE ANALYSES BELOW
give you the full nutritional details:-

OAT

Scott's Baby Cereal—Oat consists of oat flour, malt extract, bone phosphate, dried yeast, salt, iron and ammonium citrate, manganese sulphate, copper sulphate and calciferol (Vitamin D.)

	per cent.
Fat (by acid hydrolysis)	6.2
Protein (N x 6.25)	11.2
Carbohydrate	72.3
Mineral Matter	2.4
Fibre	0.6
Moisture	7.3
	per oz.
Vitamin D	600 I.U.
Vitamin B_1 (as Aneurin Hydrochloride)	0.22 mg.

	grm. per oz.
Fat (by acid hydrolysis)	1.76
Protein (N x 6.25)	3.18
Carbohydrate	20.53
	mg. per oz.
Iron	5.0
Calcium	120.0
Phosphorus	110.0
Trace Elements: Zinc	1.0
Trace Elements: Copper	0.1
Trace Elements: Manganese	0.1

Calories 114 per oz.

WHEAT

Scott's Baby Cereal-Wheat consists of wheat flour, malt extract, wheat germ, bone phosphate, calcium carbonate, dried yeast, salt, iron and ammonium citrate, manganese- sulphate and calciferol (Vitamin D.)

	per cent.
Fat (by acid hydrolysis)	2.0
Protein (N x 6.25)	14.0
Carbohydrate	72.5
Mineral Matter	2.6
Fibre	0.4
Moisture	8.5
	per oz.
Vitamin D	600 I.U.
Vitamin B_1 (as Aneurin Hydrochloride)	0.17 mg.

	grm. per oz.
Fat (by acid hydrolysis)	0.57
Protein (N x 6.25)	3.98
Carbohydrate	20.59
	mg. per oz.
Iron	5.0
Calcium	120.0
Phosphorus	100.0
Trace Elements: Zinc	0.5
Trace Elements: Copper	0.1
Trace Elements: Manganese	0.1

Calories 106 per oz.

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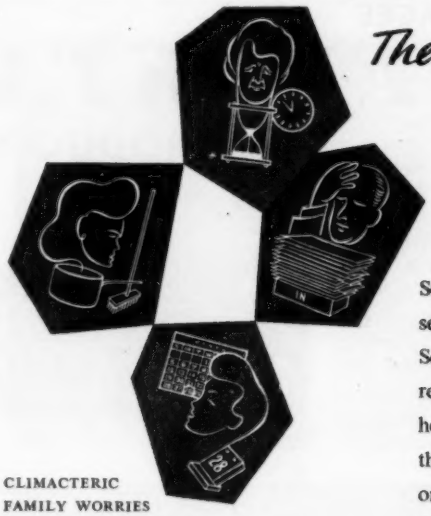

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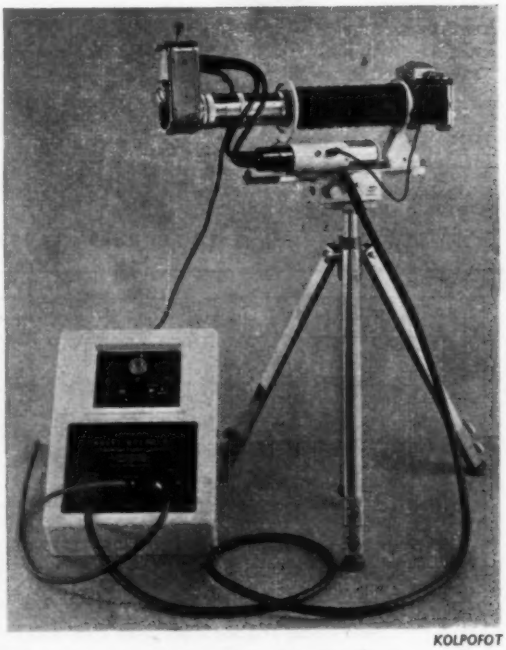

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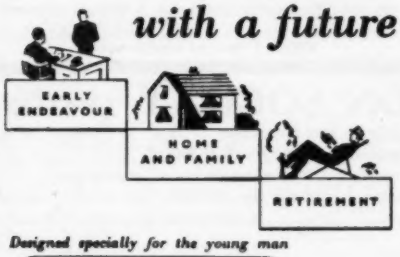

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Vacancies

ACADEMIC AND EDUCATIONAL SECTION *Page* 48

ANÆSTHETICS
Leeds United Hosps. Reg. 55
Manchester. South Manchester H.M.C. Sr. H.O. 55
Mid-Kent H.M.C. Sr. H.O. 56
Newcastle R.H.B. Cons. 49
Pembury, Kent. Sr. H.O. 57
Plymouth. South Devon & East Cornwall. Sr. H.O. 56
Scotland. South-Eastern R.H.B. Sr. Reg. & Reg. 57/58
Scotland. Western R.H.B. Reg. .. 57
Scotland. Western R.H.B. Sr. Reg... 57
South East Met. R.H.B. P.-t. Cons... 50
Taplow. Canadian Red Cross Mem. Sr. H.O. 58
Warrington Infy. Sr. H.O. 58
Welsh R.H.B. Cons. 50
Belfast H.M.C. Sr. H.O. 59
Canada. Univ. of Alberta Hosp. Anæs. 50

BACTERIOLOGY
Scotland. Western R.H.B. Sr. Reg... 57

BIOCHEMISTRY
West London, W.6. Reg. 52

CASUALTY
Hackney, E.9. H.O.'s 51
Hammersmith, West London & St. Mark's Hosps., W.12. Sr. H.O. .. 51
Prince of Wales's Gen., N.15. Prereg. H.O. 51
Royal Free, W.C.1. Sr. H.O... .. 51
Royal Northern, N.7. Reg. 51
Bebington. Clatterbridge. Jr. H.M.O. 52
Birmingham. Dudley Road. Sr. H.O. 53
Brighton Gen. H.O. 53
Cheltenham Gen. & Eye. Jr. H.M.O. 53
Hemel Hempstead. West Herts. Jr. H.M.O. 54
Maidstone. West Kent Gen. Sr. H.O. 55
Plymouth. South Devon & East Cornwall. Sr. H.O. 56
Richmond, Surrey. Royal. Sr. H.O. 57
St. Helens & Dist. H.M.C. Sr. H.O... 58
Warrington Infy. Jr. H.M.O. or H.O. or Sr. H.O. 58
Wrexham War Mem. Jr. H.M.O. .. 59

CHEST AND TUBERCULOSIS
Hammersmith, West London & St. Mark's Hosps., W.12. H.O. .. 51
Bristol. Ham Green. Sr. H.O. .. 53
Chelmsford. Broomfield. Locum Sr. H.M.O. 49
Derby. Derwent. Reg. 54
Driffield. Northfield San. Sr. H.O... 54
Henley-on-Thames. Peppard Chest. Jr. H.M.O. 55
Hexham. Wooley San. Pre-reg. H.O. or Sr. H.O. or Jr. H.M.O. 55
Ilkley. Middleton. Jr. H.M.O. .. 55
Paisley & Dist. Hosps. Jr. H.M.O. 57
Stoke-on-Trent. Stanfield San. Jr. H.M.O. 58

DENTAL SURGERY
Plymouth. South Devon & East Cornwall. H.O. 56
Scotland. Western R.H.B. Reg. .. 57

DERMATOLOGY
Scotland. Western R.H.B. Reg. .. 57

EAR, NOSE, AND THROAT
Guy's Hosp. & South East Met. R.H.B. Sr. Regs. 50
St. Mary's, W.2, & North West Met. R.H.B. P.-t. Reg. 52
Blackpool. Victoria. P.-t. Clin. Asst. 53
Derbyshire Royal Infy. Sr. H.O. .. 54
Ipswich & East Suffolk. H.O. .. 55
Maidstone. Kent County Ophthalmic & Aural. Sr. H.O. 55
Reading. Royal Berks. H.O. .. 57
Salisbury Gen. Sr. H.O. 58
South East & South West Met. R.H.B.'s. P.-t. Cons. 50
South West Met. R.H.B. P.-t. Locum Surg. 50

GERIATRICS
Ashton, Hyde & Glossop H.M.C. Sr. H.O. 52
Rochford, Essex. Gen. Sr. H.O. .. 57

HÆMATOLOGY
Newcastle R.H.B. Jr. H.M.O. .. 56

INFECTIOUS DISEASES
Paisley & Dist. Hosps. Jr. H.M.O. 57
Plymouth. Scott Isolation. H.O. .. 56

MEDICINE
Charing Cross, W.C.2. H.O.'s .. 50
Guy's Hosp. & South East Met. R.H.B. Sr. Regs. 50
Hackney, E.9. H.O. 51
Hammersmith, West London & St. Mark's Hosps., W.12. H.O.'s .. 51
Nelson, S.W.20. Sr. H.O. 51
South Lodge, N.21. H.O. 51
St. Mary's, W.2. H.O. 52
West London, W.6. H.O.'s 52
Bedford Gen. Pre-reg. H.O.'s .. 52
Birmingham Dudley Road. H.O. .. 53
Birmingham R.H.B. Regs. 52
Birmingham United Hosps. Sr. H.O. 52
Bournemouth. Royal Victoria. H.O.'s 53
Brighton. New Sussex Hosp. for Women. H.O. 53
Cambridge. Addenbrooke's. Reg. .. 53
Chelmsford. St. John's. H.O. .. 53
Driffield. East Riding Gen. H.O. .. 54
East Anglian R.H.B. Sr. Reg. .. 54
Ellesmere Port. Jr. H.M.O. 54
Enfield. War Mem. Sr. H.O. 54
Epsom Dist. Pre-reg. H.O. 54
Gainsborough. John Coupland. Jr. H.M.O. 54
Guildford. Royal Surrey Cnty. H.O. 54
Hertford County. H.O. 55
Hounslow. H.O. 55
Ipswich & East Suffolk. H.O. .. 55
Leamington Spa. Warneford Gen. Pre-reg. H.O. 55
Luton & Dunstable. Sr. H.O. .. 55
Portsmouth Group H.M.C. Pre-reg. H.O. 56
Portsmouth. St. Mary's. Sr. H.O. .. 57
Reading Area Dept. of Med. H.O. .. 57
Richmond, Surrey. Royal. Pre-reg. H.O. 57
Salisbury Gen. H.O. 58
Scotland. Western R.H.B. Reg. .. 57
St. Albans City. H.O. 58
Taplow. Canadian Red Cross Mem. Reg. 58
Torquay. Torbay. Sr. H.O. 58
Windsor. King Edward VII. H.O. .. 59
Dublin. National Child's. Reg. .. 59

NEUROSURGERY
Northern Ireland Hosps. Auth. Cons. 50

OBSTETRICS AND GYNÆCOLOGY
Charing Cross, W.C.2. H.O. 50
Guy's Hosp. & South East Met. R.H.B. Sr. Regs. 50
Hammersmith, West London & St. Mark's Hosps., W.12. H.O.'s .. 51
Queen Charlotte's & Chelsea Hosps. Sr. Reg. 51
Royal Free Hosp. Group. P.-t. Cons. 49
South London Hosp. for Women, S.W.4. H.O. 51
Bedford Gen. Pre-reg. H.O. 52
Bury & Rossendale H.M.C. Sr. H.O. 53
Hemel Hempstead. West Herts & St. Paul's Hosps. Reg. 54
Manchester R.H.B. Reg. 55
Newcastle R.H.B. Locum Reg. .. 56
North West Met. R.H.B. Reg. .. 56
Plymouth. South Devon & East Cornwall. H.O. 56
Reading Combined Hosps. H.O. .. 57
Scotland. Western R.H.B. Reg. .. 57
St. Albans City. Locum Reg. 58
Whitehaven, Cumberland. H.O. or Sr. H.O. 58

OPHTHALMOLOGY
Croydon Eye Unit. H.O. 54
Manchester United Hosps. Sr. Reg. .. 55
Romford. Oldchurch. Sr. H.O. .. 57
Scotland. Western R.H.B. Reg. .. 57
Welsh R.H.B. Sr. H.M.O. 50

ORTHOPÆDICS
Guy's Hosp. & South East Met. R.H.B. Sr. Regs. 50
Royal National Orthopædic, W.1. Sr. H.O. 51
Ashford, Middx. H.O. 52
Beverley. Westwood. H.O. 52
Brighton Gen. H.O. 53
Cardiff. Prince of Wales Orthopædic. Sr. H.O. 53
Carmarthen. West Wales Gen. Sr. H.O. 54
Doncaster Royal Infy. Reg. 54
Kingston, Surrey. Locum Sr. H.O. .. 55
Paisley & Dist. Hosps. Jr. H.M.O. 57
Portsmouth Group H.M.C. Pre-reg. H.O. 56
Romford. Oldchurch. H.O. 57
Rotherham. Reg. 57
Southend Gen. Temp. Sr. H.O. .. 58
Stoke-on-Trent. North Staffs Royal Infy. Sr. H.O. 58
Wakefield. Pinderfields Gen. Sr. H.O. 58
Welsh R.H.B. Sr. H.M.O. 50

PÆDIATRICS
Hammersmith, West London & St. Mark's Hosps., W.12. H.O. .. 51
St. Mary's, W.2. Reg. 52
Birmingham. Marston Green Maty. Sr. H.O. 52
Birmingham United Hosps. Reg. .. 53
Brighton. Royal Alexandra Hosp. for Sick Child. Sr. H.O. & H.O. .. 53
Bury & Rossendale H.M.C. Sr. H.O. 53
Edgware Gen. H.O. 54
Leeds United Hosps. Sr. H.O. .. 55
Newcastle R.H.B. Reg. 56
Portsmouth Group H.M.C. Sr. H.O. .. 56
Scotland. South-Eastern R.H.B. Sr. Reg. 58
Scotland. Western R.H.B. Reg. .. 57

PATHOLOGY
Bethnal Green, E.2. Sr. H.O. .. 50
Guy's Hosp. & South East Met. R.H.B. Sr. Regs. 50
Royal Marsden, S.W.3. Sr. H.M.O. .. 49
St. John's Hosp. for Diseases of Skin, W.C.2. Reg. 52
Beverley. Westwood. Sr. H.O. .. 52
Birmingham R.H.B. Cons. 49
Birmingham R.H.B. Reg. 52
Edgware Gen. Sr. H.O. 54
Manchester R.H.B. Reg. 55
Oxford United Hosps. Sr. H.O.'s .. 56
Rotherham Clinical Lab. Reg. .. 57
Sheffield. City Gen. Reg. & Sr. H.O. 57
Sheffield United Hosps. Reg. or Sr. H.O. 57
Welsh R.H.B. Cons. 50

PHYSICAL MEDICINE
Guy's Hosp. & South East Met. R.H.B. Sr. Regs. 50

PLASTIC SURGERY
East Anglian R.H.B. Reg. 54

PSYCHIATRY
Charing Cross Hosp. Group. Reg. .. 50
Guy's Hosp. & South East Met. R.H.B. Sr. Regs. 50
Birmingham. Monyhull Hall. Jr. H.M.O. 52
Birmingham R.H.B. Cons. 49
Bristol Mental H.M.C. Jr. H.M.O. .. 53
Liverpool United Hosps., R.H.B. & Univ. P.-t. Cons. 49
Newcastle R.H.B. Cons. 49
Newcastle United Hosps. Sr. Reg. .. 56
North West Met. R.H.B. Sr. H.M.O. 49
Oxford R.H.B. Reg. 56
Scotland. Western R.H.B. Reg. .. 57
Welsh R.H.B. Reg. 58
West Malling. Leybourne Grange Colony for Mental Defectives. Jr. H.M.O. 58
Wickford, Essex. Runwell. Sr. H.O. 58
Woodford Bridge, Essex. Claybury. Sr. H.O. 58

RADIOLOGY
Charing Cross, W.C.2. H.O. 50
Guy's Hosp. & South East Met. R.H.B. Sr. Regs. 50
St. Mary's, W.2. P.G. Traineeship (Sr. H.O.) 52
Brighton & Lewes H.M.C. P.-t. Locum 49
Croydon Gen. Locum Cons. 49
Manchester R.H.B. Cons. & Sr. H.M.O. 49
Scotland. Western R.H.B. Sr. H.M.O. 49
South West Met. R.H.B. P.-t. Locum 50
Belfast H.M.C. Sr. H.O. 59

RADIOTHERAPY
Hammersmith Hosp. & P.G. Med. School, W.12. Sr. Reg. 51
Hammersmith, West London & St. Mark's Hosps., W.12. H.O. .. 51
Sheffield R.H.B. Sr. H.M.O. 50

SURGERY
Bolingbroke, S.W.11. H.O.'s .. 50
Charing Cross Hosp. Group. Reg. .. 50
Charing Cross, W.C.2. H.O.'s .. 50
Connaught, E.17. H.O.'s 51
Guy's Hosp. & South East Met. R.H.B. Sr. Regs. 50
Hosp. of St. John & St. Elizabeth, N.W.8. Reg. & H.O. 51
Lambeth, S.E.11. H.O. 51
North Middlesex, N.18. Sr. H.O. .. 51
Queen Mary's Hosp. for the East End, E.15. Pre-reg. H.O. 51
Royal Marsden, S.W.3. H.O. .. 51
South London Hosp. for Women, S.W.4. Locum H.O. 51
St. Ann's Gen., N.15. H.O. 51
St. Ann's Gen., N.15. Sr. H.O. .. 51
St. Mary's Hosp. for Women & Child., E.13. Pre-reg. H.O. 52
Bedford Gen. Pre-reg. H.O.'s .. 52
Bexhill, Sussex. Pre-reg. H.O. .. 52
Birmingham Accident. H.O. 52
Birmingham. Solihull. Pre-reg. H.O. 53
Brighton Gen. H.O. 53
Brighton. Royal Alexandra Hosp. for Sick Child. H.O. 53
Brighton. Royal Sussex County. H.O. 53
Bristol. Cossham & Frenchay H.M.C. H.O. 53
Bury & Rossendale H.M.C. Sr. H.O. 53
Cardiff. Royal Hamadryad Gen. & Seamen's. Sr. H.O. 53
Chelmsford & Essex. Pre-reg. H.O. 53
Chelmsford. St. John's. H.O. .. 53
Chesterfield Royal. H.O. 53
Chester-le-Street. Gen. Sr. H.O. .. 53
Chichester. Royal West Sussex. H.O. 53
Clacton & Dist. Reg. (Temp.) .. 54
Croydon Gen. Pre-reg. H.O. 54
Croydon. Mayday. Pre-reg. H.O. .. 53
Dorking Gen. Sr. H.O. 54
East Anglian R.H.B. Reg. 54
Enfield. Chase Farm. H.O. 54
Epsom Dist. Pre-reg. H.O. 54
Glasgow. Southern Gen. Sr. H.O. 54
Guildford. Royal Surrey Cnty. H.O. 54
Hastings. Royal East Sussex. Pre-reg. H.O. 54
Hereford County. H.O. 54
Hounslow. H.O. 55
Hove. Gen Sr. H.O. 55
Huddersfield Royal Infy. H.O. .. 54
Ilford. King George. Pre-reg. H.O.'s 55
Ipswich & East Suffolk. H.O. .. 55
Maidenhead. Reg. 55
Manchester. Christie Hosp. & Holt Radium Inst. Sr. H.O. 55
Manchester R.H.B. Regs. .. 55/56
Manchester United Hosps. Sr. H.O.'s 55
Manchester. Wythenshawe. Sr. H.O. 56
Middlesbro. Hemlington. Sr. H.O. 56
Nottingham City. Sr. H.O. & H.O. 56
Nottingham Gen. H.O.'s 56
Plymouth. South Devon & East Cornwall. Sr. H.O.'s & Pre-reg. H.O.'s 56
Poole Gen. Pre-reg. H.O.'s 56
Portsmouth Group H.M.C. Pre-reg. H.O.'s 56
Reading. Royal Berks. H.O. .. 57
Redhill. East Surrey. Sr. H.O. .. 57
Richmond, Surrey. Royal. Pre-reg. H.O. 57
Romford. Victoria. Temp. Reg. .. 57
Salisbury Gen. H.O. 58
Scotland. Western R.H.B. Reg. .. 57
Southampton. Royal South Hants & Gen. H.O.'s. 58
St. Albans City. Locum Reg. .. 58
Stoke-on-Trent. North Staffs Royal Infy. Pre-reg. H.O. 58
Welsh R.H.B. Sr. Reg. & Regs. .. 58
Winchester. Royal Hants Cnty. H.O. 59
Belfast H.M.C. Sr. H.O. 59
Channel Islands, Jersey. Gen. R.S.O. 59

THORACIC SURGERY
Hosps. for Diseases of the Chest. Sr. Reg. 51
London Chest, E.2. Reg. 51

VENEREOLOGY
Guy's Hosp. & South East Met. R.H.B. Sr. Reg. 50
St. Mary's, W.2. Reg. 52

GENERAL
Northern Ireland Hosps. Auth. Sr. Regs., Regs. & Sr. H.O.'s 59

PUBLIC APPOINTMENTS 59

GENERAL PRACTICE 60

NON-MEDICAL 60

MISCELLANEOUS 60

Academic and Educational

ROYAL COLLEGE OF SURGEONS OF ENGLAND

COUNCIL ELECTION

Tuesday, 17th April, was the last day on which the names of candidates were to be received for the election of Members of the Council, which will take place on 5TH JULY. 3 nominations have been forwarded to the Secretary by candidates seeking to fill the 2 vacancies occasioned by the retirement, in rotation, of Sir Russell Brock and Sir Archibald McIndoe.

1. Sir Russell Claude Brock (Fellow 1929). Guy's Hospital Council 1948–56.
2. Sir Archibald Hector McIndoe, C.B.E. (Fellow 1932). St. Bartholomew's Hospital. Council 1948–56.
3. Rodney Honor Maingot (Fellow 1920). Royal Free Hospital.

KENNEDY CASSELS, Secretary.

ROYAL COLLEGE OF PHYSICIANS OF LONDON

CHARLES MURCHISON SCHOLARSHIP IN CLINICAL MEDICINE

The next EXAMINATION for the Scholarship will be held in London on FRIDAY, 6TH JULY, 1956.

The Examination is open to any student of medicine, whether holding a medical qualification or not, who, subsequently to the date of passing his professional Examination in Anatomy and Physiology for a medical qualification, commenced clinical studies not less than 2½ and not more than 5 years previously at a medical school in London, recognised by the Royal College of Physicians, or at the University of Edinburgh, including medical classes recognised by the Medical Faculty of the University.

The Scholarship is of the value of 20 guineas and is tenable for 1 year.

Intending candidates are required to send their names to the Registrar of the Royal College of Physicians, 12, Pall Mall East, London, S.W.1, not later than first post on Friday, 15th June, 1956, with evidence of the duration of their medical studies from the Deans of their respective Schools and evidence of the date at which they passed their Examination in Anatomy and Physiology.

HAROLD BOLDERO, D.M., Registrar.

12, Pall Mall East, London, S.W.1.

ROYAL COLLEGE OF PHYSICIANS OF LONDON

The next EXAMINATION for the MEMBERSHIP will commence on MONDAY, 25TH JUNE, 1956.

Prospective candidates are asked to note that entries accompanied by the certificates, testimonials and the Examination fee of 15 guineas as required by the bylaws, must reach the College not later than first post on Monday, 28th May, 1956. Candidates must have been qualified for 18 months.

Candidates who propose to submit Published Work under the regulations are required to give 28 days notice, and should apply in writing to the Registrar, without delay, for detailed instructions as to the procedure they should follow. Completed entries for Published Work must also reach the College not later than first post on Monday, 28th May, 1956.

HAROLD BOLDERO, D.M., Registrar.

12, Pall Mall East, London, S.W.1.

UNIVERSITY OF MANCHESTER

FACULTY OF MEDICINE

DIPLOMA IN PUBLIC HEALTH

A PART-TIME COURSE covering 2 academic years will commence in OCTOBER, 1956. Candidates are required to obtain posts in the Manchester region from which they are permitted to attend the University for the equivalent of 2½ days each week for 6 terms. Every assistance is given to prospective candidates to obtain suitable employment.

Application forms may be obtained from the Dean of Postgraduate Medical Study, University of Manchester, Manchester, 13, or from Prof. C. F. BROCKINGTON, Department of Social and Preventive Medicine, Clinical Sciences Building, Yorkplace, Manchester, 13.

THE UNIVERSITY OF MANCHESTER

SYBIL MARY PILKINGTON FELLOWSHIP FOR RESEARCH INTO DISEASES OF THE BLOOD

Applications are invited for the Sybil Mary Pilkington Fellowship for research into Diseases of the Blood, with particular reference to the causation, treatment and cure of leukæmia in man. The Fellowship is open to persons who have obtained a medical qualification registrable in the United Kingdom, the Dominions or any other country. It is of the normal value of £700 p.a. and is tenable for 1 year in the first instance, but may be renewed for a second or subsequent years.

Applications must be sent not later than 1st June, 1956, to the Registrar, the University, Manchester, 13, from whom further particulars and forms of application may be obtained.

DENTAL AND MEDICAL SOCIETY FOR THE STUDY OF HYPNOSIS

The next INTENSIVE WEEKEND COURSE to be held by the Society will be on SATURDAY, 26TH MAY and SUNDAY, 27TH MAY. This Study Group is intended for members who do not reside in the London area.

The next Full Course to be held will begin on TUESDAY, 5TH JUNE, and will run for 7 consecutive Tuesdays. This Study Group includes individual tuition.

Details may be obtained from the Secretary, Mr. DAWSON WATTS, 22, Gordon-road, Ealing, W.5.

SOCIETY OF APOTHECARIES OF LONDON

DIPLOMA IN INDUSTRIAL HEALTH

The next Examination will begin on MONDAY, 2ND JULY, 1956. The following Examination will be held in December, 1956.

For Regulations apply Registrar, Apothecaries' Hall, Black Friars-lane, London, E.C.4.

UNIVERSITY OF LONDON

A LECTURE on "Factors in the Control of Movement" will be given by Dr. S. W. KUFFLER (Johns Hopkins Hospital) at 5.30 P.M., on 8TH MAY at University College (Physiology Theatre), Gower-street, W.C.1.

Admission free, without ticket.

JAMES HENDERSON, Academic Registrar.

UNIVERSITY OF LONDON

A LECTURE on "Post-denervation Supersensitivity" will be given by Prof. F. A. SIMEONE (Western Reserve University) at 5 P.M., on 4TH MAY at St. Bartholomew's Hospital Medical College, Physiology Lecture Theatre, Charterhouse-square.

Admission free, without ticket.

JAMES HENDERSON, Academic Registrar.

THE WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY

ST. MARY'S HOSPITAL MEDICAL SCHOOL, London, W.2

A Course of 6 ALMROTH WRIGHT LECTURES has been arranged for the SUMMER SESSION, 1956. These Lectures will be given on the following dates in the Lecture Theatre of this Institute at 5 P.M.

Tuesday, 8th May
Prof. L. PILLEMER (Western Reserve University, Cleveland, Ohio, U.S.A.) — "The Nature of the Properdin System."

Tuesday, 15th May
Dr. W. E. VAN HEYNINGEN (Sir William Dunn School of Pathology, University of Oxford) — "Recent Trends in Research on Bacterial Toxins."

Tuesday, 22nd May
Prof. F. W. ROGERS BRAMBELL (Department of Zoology, University College of North Wales, Bangor) — "Transmission of Passive Immunity."

Tuesday, 29th May
Dr. R. E. O. WILLIAMS (Central Public Health Laboratory, Colindale, N.W.9) — "The Numbers and Significance of Bacteria in Air."

Tuesday, 5th June
Prof. C. H. STUART-HARRIS (University Department of Medicine, Sheffield) — "Recent Studies in Acute Respiratory Disease."

Tuesday, 12th June
Prof. R. HARE (Bacteriology Department, St. Thomas's Hospital) — "The Transmission of Infections of the Respiratory Tract."

These Lectures are open to all members of the Medical Profession and to all Students in Medical Schools without fee.

DICKINSON SCHOLARSHIPS

Applications are invited for a TRAVELLING SCHOLARSHIP IN MEDICINE, up to the value of £1000, tenable for 1 year.

Candidates must be graduates of any University who have taken their full course of instruction in medicine and surgery at the University of Manchester and at the Manchester Royal Infirmary.

Copies of the regulations governing the Scholarships may be obtained from the undersigned, to whom 6 copies of application should be sent not later than 31st May, 1956.

G. H. TAYLOR,
Secretary to the Dickinson Scholarship Trustees.
Manchester Royal Infirmary, Manchester, 13.

DICKINSON SCHOLARSHIPS

Applications are invited for a SCHOLARSHIP IN SURGERY value £75.

Candidates must be graduates of any University who have taken their full course of instruction in medicine and surgery at the University of Manchester and at the Manchester Royal Infirmary.

Copies of the regulations governing the Scholarships may be obtained from the undersigned, to whom 6 copies of application should be sent not later than 31st May, 1956.

G. H. TAYLOR,
Secretary to the Dickinson Scholarship Trustees.
Manchester Royal Infirmary, Manchester, 13.

DICKINSON SCHOLARSHIPS

Applications are invited for a SCHOLARSHIP IN PATHOLOGY, value £75.

Candidates must be graduates of any University who have taken their full course of instruction in medicine and surgery at the University of Manchester and at the Manchester Royal Infirmary.

Copies of the regulations governing the Scholarships may be obtained from the undersigned, to whom 6 copies of application should be sent not later than 31st May, 1956.

G. H. TAYLOR,
Secretary to the Dickinson Scholarship Trustees.
Manchester Royal Infirmary, Manchester, 13.

UNIVERSITY OF BRISTOL. Applications are invited for the appointment of LECTURER AND HEAD of the Department of Anæsthetics in the University, tenable in the United Bristol Hospitals. Salary within the scale for Clinical Lecturers, together with superannuation and children's allowances. The successful candidate will be granted an honorary contract as Consultant with the Board of Governors of the United Bristol Hospitals.

Applications (20 copies), stating age, qualifications and experience and including the names of 3 referees, should reach the undersigned, from whom further particulars may be obtained, not later than 22nd May, 1956.

H. C. BUTTERFIELD, Registrar and Secretary.

UNIVERSITY OF LONDON. The Senate invite applications for the CHAIR OF MEDICAL ENTOMOLOGY tenable at the London School of Hygiene and Tropical Medicine (salary within range £2250–£2850 a year).

Applications (10 copies) must be received not later than 30th July, 1956, by the Academic Registrar, University of London, Senate House, W.C.1, from whom further particulars may be obtained.

THE ROYAL FREE HOSPITAL. Applications are invited for the whole-time or part-time post of RESEARCH SCHOLAR IN CLINICAL CHEMICAL PATHOLOGY. Candidates must be medically qualified and have held clinical appointments: previous experience of laboratory work would be an advantage. The appointment is for 1 year in the first instance, at a salary of £750 p.a. (or proportionately for part-time) and is to begin on 1st May, 1956, or shortly after.

Applications, accompanied by the names of 2 referees, should be sent to the Secretary, Royal Free Hospital, Gray's Inn-road, W.C.1 (from whom further particulars may be obtained) as soon as possible.

UNIVERSITY OF GLASGOW. Applications are invited for a LECTURESHIP IN PATHOLOGY at the Royal Infirmary. Salary according to placement on University scale for clinical teachers. The final maximum is £1750 p.a. F.S.S.U. and family allowance benefits.

Applications (12 copies) should be lodged, not later than 19th May, 1956, with the undersigned, from whom further particulars may be obtained.

ROBT. T. HUTCHESON, Secretary of University Court.

UNIVERSITY OF BELFAST. The Senate of the Queen's University of Belfast invites applications from graduates in medicine for a LECTURESHIP IN MICROBIOLOGY from 1st October, 1956. Special experience in virus diseases is essential. Salary £1300–£50–£1950 with provisions for superannuation. In certain circumstances the salary may rise to £2250. Initial placing on the scale will depend on experience and qualifications.

Applications should be submitted by 30th May, 1956. Further particulars from G. R. COWIE, M.A., LL.B., Secretary.

THE UNIVERSITY OF SHEFFIELD. Applications are invited for a post of SENIOR LECTURER or LECTURER IN BIOCHEMISTRY, to begin duties on 1st September, 1956, or as soon as possible thereafter. Salary scales: (*a*) for candidates holding a registered medical qualification—Senior Lecturer £1750–£100–£2050, Lecturer £1000–£100–£1700; (*b*) for other candidates—Senior Lecturer £1400–£50–£1650, Lecturer £650–£50–£1350. Commencing salary in either grade according to qualifications and experience, with F.S.S.U. provision and family allowance.

Applications (8 copies) should be sent to the Registrar, from whom further particulars may be obtained by 26th May, 1956.

SOCIAL MEDICINE RESEARCH UNIT of Medical Research Council has vacancy for STATISTICIAN. Applications are invited from medically qualified, or other persons. In the latter case applicants should have some experience, or a good relevant degree and an interest in medical and social problems. Salary in accordance with qualifications and experience; child allowances; superannuation; good long term prospects.

Please write to Dr. J. N. MORRIS, Research Laboratories, London Hospital, Ashfield-street, London, E.1.

Hospital Services: Senior Appointments

ROYAL FREE HOSPITAL GROUP. Elizabeth Garrett ANDERSON HOSPITAL. Applications are invited from Women registered medical practitioners for the appointment of CONSULTANT OBSTETRICIAN AND GYNÆCOLOGIST. The appointment is for 4 sessions per week, commencing on 1st October, 1956. Terms and conditions of service as laid down by the Ministry of Health.

Applications, stating details of qualifications, experience, and giving the names of 3 referees, should be forwarded to the Secretary to the Board of Governors, Royal Free Hospital, Gray's Inn-road, W.C.1, not later than 11th May, 1956.

ROYAL MARSDEN HOSPITAL, Fulham-road, London, S.W.3. Applications are invited for the post of Full-time ASSISTANT PATHOLOGIST (Senior Hospital Medical Officer grade) in the Department of Pathology (Morbid Anatomy).

Applications (12 copies), together with names of 3 referees, should be sent to the House Governor to reach him not later than 14th May, 1956.

BIRMINGHAM REGIONAL HOSPITAL BOARD.

Birmingham (Dudley Road) Group of Hospitals

Whole-time CONSULTANT PATHOLOGIST responsible for group pathological services and for general coördination of laboratory work. Duties mainly at Dudley Road Hospital, Birmingham. Higher qualification/wide experience specialty essential.

All Saints' Hospital, Winson Green, including early Treatment Centre, Ufficulme (1358 Beds)

Whole-time CONSULTANT PSYCHIATRIST AND DEPUTY MEDICAL SUPERINTENDENT. Higher qualification and experience specialty essential. Non-resident.

Applications (15 copies), stating name, age, qualification, nationality, present and previous appointments, and details of 3 referees, to Secretary, 10, Augustus-road, Birmingham, 15, before 14th May, 1956.

BRIGHTON AND LEWES HOSPITAL MANAGEMENT COMMITTEE. Locum RADIOLOGIST from 27th August to 22nd September, 1956. 9 notional half-day sessions a week at hospitals in Brighton.

Applications, stating usual particulars, together with names and addresses of 2 referees, to Group Secretary, Brighton and Lewes Hospital Management Committee, Royal Sussex County Hospital, Brighton.

CHELMSFORD, ESSEX. BROOMFIELD HOSPITAL. Required experienced Locum Tenens SENIOR HOSPITAL MEDICAL OFFICER (part resident). Unit has 330 Beds for the treatment of pulmonary tuberculosis in adults. Tuberculous and non-tuberculous thoracic surgery. Chest clinics and mass radiography.

Apply Physician-Superintendent.

CROYDON GENERAL HOSPITAL. (200 Beds.) Locum Tenens CONSULTANT RADIOLOGIST (full-time), 9th–20th July inclusive and 20th August–7th September, inclusive.

Applications to— GEORGE A. PAINES, Group Secretary, Hospital Management Committee.

General Hospital, London-road, Croydon.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. LIVERPOOL REGIONAL HOSPITAL BOARD. THE UNIVERSITY OF LIVERPOOL. Applications are invited for a joint appointment as CONSULTANT PSYCHIATRIST (child psychiatry) (for 7 notional half-days) to The United Liverpool Hospitals and the Liverpool Regional Hospital Board, and LECTURER in Child Psychiatry in the Department of Studies in Psychological Medicine of the University of Liverpool. The appointment is for 3 notional half-days a week for duty in The United Liverpool Hospitals, in the first instance as Consultant in charge of the Department of Psychiatry in the Royal Liverpool Children's Hospital, and for 4 notional half-days a week for duty with the Liverpool Regional Hospital Board, in the first instance at Alder Hey Children's Hospital. In the University Department duties will be in connection with the undergraduate and post-graduate courses in psychological medicine and the person appointed will be remunerated for these by the University at the rate of £200 p.a. Candidates must possess a registrable qualification, and the M.D. of a University of the British Commonwealth or M.R.C.P. (London, Edinburgh or Ireland), and a special qualification in psychiatry.

Applications, giving full particulars of age, qualifications and details of present and previous appointments together with the names of 3 persons to whom reference may be made, should reach the Secretary (from whom further particulars may be obtained), The United Liverpool Hospitals, 80, Rodney-street, Liverpool, 1, by 12th May, 1956.

MANCHESTER REGIONAL HOSPITAL BOARD.

(*a*) Whole-time or maximum Part-time Additional CONSULTANT RADIOLOGIST to the Ashton, Hyde and Glossop Group of hospitals (mainly Ashton-under-Lyne General Hospital, near Manchester (677 Beds), &c.). Wide experience and higher qualifications essential, appointee to reside in area. 16th May, 1956.

(*b*) Whole-time NON-RESIDENT ASSISTANT RADIOLOGIST (Senior Hospital Medical Officer) to the North Manchester Hospitals (Ancoats, Manchester Victoria Memorial Jewish, Manchester Northern and Crumpsall Hospitals) and at Booth Hall (Children's) and Monsall Hospitals and Prestwich (Mental) Hospital. Successful candidate will work under general guidance of Consultants in wide range of radiological investigations, including specialised pædiatrics, neurosurgical and cardiological. Wide experience of diagnostic radiology and D.M.R.D. essential. 17th May, 1956.

Application forms from the Senior Administrative Medical Officer to the Board, Cheetwood-road, Manchester, 8, to be returned by dates stated.

NEWCASTLE REGIONAL HOSPITAL BOARD. WINTERTON HOSPITAL, SEDGEFIELD. (2048 Beds.) CONSULTANT PSYCHIATRIST (whole-time, or maximum part-time). Resident, a suitable house is available. The Hospital serves the County Borough of Darlington, Hartlepool, and part of the County of Durham (population 786,037). Applicants must have had wide experience in psychiatry and be competent to take clinical responsibility, subject to the general administrative control of the Medical Superintendent, of a section of the Hospital and to participate in the work of the associated outpatient clinics, &c. Further particulars from Regional Psychiatrist.

Applications, with names and addresses of 3 referees, to Regional Psychiatrist, Walker Gate Hospital, Benfield-road, Newcastle upon Tyne, 6, within 28 days.

NEWCASTLE REGIONAL HOSPITAL BOARD. Gateshead DISTRICT HOSPITAL MANAGEMENT COMMITTEE AREA. (Main hospitals: Queen Elizabeth (176 Beds), Bensham General (230 Beds), Dunston Hill (300 Beds).) CONSULTANT ANÆSTHETIST, whole-time or maximum part-time for 9 notional half-days per week. (Initially, as a temporary measure, the appointee may be required to devote approximately half of his time to sessions in the Newcastle Group of hospitals.)

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Walker Gate Hospital, Benfield-road, Newcastle upon Tyne, 6, within 28 days.

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. ASSISTANT PSYCHIATRIST (whole-time), Senior Hospital Medical Officer grade, Cell Barnes Hospital, St. Albans (676 Beds—Mental Deficiency). Duties will include those of Deputy Medical Superintendent. Hospital may be visited by direct appointment.

Application forms obtainable from, and returnable to, Secretary, North West Metropolitan Regional Hospital Board, 11a, Portland-place, W.1, before 4th June, 1956.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of Whole-time ASSISTANT RADIOLOGIST based at the Western Infirmary, Glasgow. Salary (at age 32 and over) on the scale £1500–£50–£1950. This appointment is subject to the National Health Service (Scotland) superannuation regulations.

Applications (16 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, not later than 30 days after publication of this advertisement.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time ASSISTANT RADIOTHERAPIST for the Sheffield National Centre for Radiotherapy. Candidates should be in possession of the D.M.R.(T.). The successful applicant will work under the direction of the Medical Director. Salary scale £1500–£50–£1950.

Application forms and further details from the Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 19th May, 1956.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited to fill a vacancy for a CONSULTANT ANÆSTHETIST to undertake 3 notional half-days a week in the Bromley Group of hospitals to include the following sessions at Farnborough Hospital, travel time and emergencies :—

Mondays A.M.—orthopædic surgery.
Tuesdays P.M.—general surgery.
Saturdays A.M.—E.N.T. surgery.

Candidates must have had wide experience in anæsthetics and hold the qualification of F.F.A.R.C.S. Applicants may visit the hospitals concerned.

Apply, stating nationality, age, sex, qualifications and experience, including details of present appointment and of war service, together with the names and addresses of 3 referees, to the Secretary, Advisory Appointments Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 19th May, 1956.

SOUTH EAST AND SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARDS. Applications are invited for an appointment as Part-time CONSULTANT in E.N.T. Surgery for 8 notional half-days a week, in the Brighton and Lewes, Mid-Sussex, and Worthing Groups of hospitals. Candidates must have had wide experience in E.N.T. surgery and be Fellows of a Royal College of Surgeons. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales). Candidates may visit the hospitals concerned.

Apply, stating nationality, age, sex, qualifications and experience, including details of present appointment and of war service, together with the names and addresses of 3 referees, to the Secretary, Advisory Appointments Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, London, W.1, not later than 19th May, 1956.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires a Locum Tenens E.N.T. SURGEON for 8 half-days per week for the Isle of Wight Group of hospitals from 9th to 29th May inclusive. Remuneration will be in accordance with the terms and conditions of service of hospital medical staff.

Applications, stating age, qualifications and experience, and names and addresses of 2 referees, to the Area Secretary, Highcroft, Romsey-road, Winchester, by 3rd May, 1956.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires a Locum Tenens RADIOLOGIST for 9 half-days per week for the Salisbury Group of hospitals from 26th May to 23rd June, inclusive. Remuneration will be in accordance with the terms and conditions of service of hospital medical staff.

Applications, stating age, qualifications and experience, and names and addresses of 2 referees, to the Area Secretary, Highcroft, Romsey-road, Winchester, by 14th May, 1956.

WELSH REGIONAL HOSPITAL BOARD. Consultant PATHOLOGIST required Cardiff Hospital Management Committee area. Duties of appointment include visits to certain main hospitals in Group. Optional whole-time/maximum part-time appointment.

Applications, naming 3 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 21 days.

WELSH REGIONAL HOSPITAL BOARD. Whole-time ASSISTANT TRAUMATIC SURGEON (Senior Hospital Medical Officer), East Glamorgan Hospital, Church Village, Glam (316 Beds). Successful candidate will work under direction of Consultant staff.

Applications (12 copies), naming 3 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 21 days.

WELSH REGIONAL HOSPITAL BOARD. Whole-time ASSISTANT OPHTHALMOLOGIST (Senior Hospital Medical Officer scale), Newport and East Mon Hospital Management Committee area. Based at Royal Gwent Hospital, Newport (260 Beds). Duties include visits to other hospitals within neighbouring Hospital Management Committee Groups. Post recognised for F.R.C.S., in Ophthalmology (6 months) and D.O. Successful candidate will work under Consultants in charge. Non-resident.

Applications, naming 3 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 21 days.

NORTHERN IRELAND HOSPITALS AUTHORITY. Applications are invited for the post of CONSULTANT NEUROSURGEON with headquarters at the Royal Victoria Hospital, Belfast. The terms and conditions will be in accordance with the application of the Spens report to Northern Ireland.

Applications to be made on a form obtainable (with further particulars) from the Secretary, Northern Ireland Hospitals Authority, 44–46, Queen-street, Belfast, and to be returned not later than 16th May, 1956.

CANADA. UNIVERSITY OF ALBERTA HOSPITAL, EDMONTON, CANADA, requires ANÆSTHETIST. Starting salary for individual with 2 years postgraduate training $7350 p.a., D.A. $8350 p.a. 3 annual increments of $500 after Canadian certification obtained. Generous provision for sick benefits, vacation and pension. Transportation loan available if desired.

Apply giving references, photograph, first letter to the Medical Superintendent.

WELSH REGIONAL HOSPITAL BOARD. Consultant ANÆSTHETIST to serve Merthyr and Aberdare Hospital Management Committee. Based at Merthyr General Hospital. Visits to other hospitals in Group and hospitals in neighbouring Hospital Management Committee areas. F.F.A.R.C.S. essential. Successful applicant required reside within Hospital Management Committee area. Optional whole-time/maximum part-time appointment.

Applications (12 copies) naming 3 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 21 days.

Hospital Services : Junior Appointments

BETHNAL GREEN HOSPITAL, Cambridge Heath-road, London, E.2. (Acute 309 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (pathology), resident or non-resident, for area laboratory at this Hospital. The successful candidate will be expected when necessary to work in other hospitals in the Group under the supervision of the area Pathologist.

Applications, stating age, nationality, experience, and qualifications, with copies of 3 recent testimonials, to the Hospital Secretary, immediately.

BOLINGBROKE HOSPITAL, Wandsworth Common, S.W.11. HOUSE SURGEONS (2), resident, required from 21st and 23rd May, 1956. Open to registered practitioners and pre-registration candidates.

Apply Hospital Secretary, enclosing copies of 3 recent testimonials, by 1st May, 1956.

CHARING CROSS HOSPITAL, W.C.2. Applications are invited for the following pre-registration appointments tenable for 6 months from 1st July, 1956 :—

(*a*) **Charing Cross Hospital**
HOUSE PHYSICIAN to the Radiological Department.
(*b*) **Mount Vernon Hospital**
HOUSE SURGEON to the Gynæcological Department.
HOUSE PHYSICIAN.
HOUSE SURGEON.
(*c*) **Harrow Hospital**
1 HOUSE PHYSICIAN.
2 HOUSE SURGEONS.
(*d*) **Wembley Hospital**
1 HOUSE PHYSICIAN.
3 HOUSE SURGEONS.

Application forms to be returned to the undersigned by 14th May, 1956.

FRANK HART, House Governor and Secretary to the Board.

CHARING CROSS HOSPITAL GROUP. Full-time REGISTRAR (resident) in the Department of Psychological Medicine. Duties in Charing Cross Psychiatric Unit at Wembley Hospital, involving modern physical treatments and psychotherapy for inpatients and outpatients.

Applications, on forms obtainable from the undersigned, to be submitted by 21st May, 1956.

FRANK HART, House Governor and Secretary to the Board.

CHARING CROSS HOSPITAL GROUP. Wembley HOSPITAL. (134 Beds.) Applications are invited for the post of SURGICAL REGISTRAR (resident) tenable at Wembley Hospital for 1 year in the first instance from 1st June, 1956. Candidates should hold the Diploma of F.R.C.S. Salary and conditions in accordance with National Health Service regulations.

Applications, with copies of testimonials and names of 2 referees, should be sent to the undersigned, immediately.

FRANK HART, Secretary to the Board of Governors.
Charing Cross Hospital, London, W.C.2.

GUY'S HOSPITAL AND SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited to fill an established vacancy as SENIOR REGISTRAR in Venereology to the Board of Governors of Guy's Hospital and the South East Metropolitan Regional Hospital Board. The holder will be expected to divide his time between the 2 hospitals concerned during a 4-year tenure of the post. The appointment will be made jointly by the bodies concerned and will be held at Guy's Hospital and in the Regional Hospital in the Seamen's Group. The post, which will be reviewed annually, is subject to the terms and conditions of service of hospital medical and dental staffs (England and Wales) with duties commencing on a date to be arranged.

Forms of application are obtainable from, and should be lodged with, the Superintendent, Guy's Hospital, London Bridge, S.E.1, not later than 24th May.

GUY'S HOSPITAL AND SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited to fill the following established vacancies for SENIOR REGISTRARS to the Board of Governors of Guy's Hospital and the South East Metropolitan Regional Hospital Board. They will be expected to spend a minimum of 1 and not more than 2 years in a Regional Board Hospital, in the Group as stated, on an exchange basis during a 4-year tenure of the post. The appointments will be made jointly by the bodies concerned and will be held in the first instance at Guy's Hospital. The posts, which will be reviewed annually, are subject to the terms and conditions of service of hospital medical and dental staffs (England and Wales), with duties commencing on 1st October, 1956.

General Medicine—Bromley Group.
General Surgery—South-East Kent Group.
Obstetrics and Gynæcology—Bromley Group.
Psychological Medicine—Bexley Group.
E.N.T. Surgery—Bromley Group.
Orthopædic and Traumatic Surgery—Medway and Gravesend Group.
Clinical Pathology—Lewisham Group.
Diagnostic Radiology—Bromley Group.
Physical Medicine—Bromley Group.

Forms of application are obtainable from, and should be lodged with, the Superintendent, Guy's Hospital, London Bridge, S.E.1, not later than 24th May, 1956.

CONNAUGHT HOSPITAL, Walthamstow, E.17. (118 Beds.) 2 HOUSE SURGEONS required for 6 months (General Surgery and Special Departments). Posts vacant 18th and 31st May, 1956. Recognised for F.R.C.S.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Hospital Management Committee, Forest Group, Langthorne-road, E.11.

HACKNEY HOSPITAL, London, E.9. (General—841 Beds.) Applications for 6 months appointment of registered HOUSE PHYSICIAN from 1st June, 1956, should be sent by 5th May, 1956, to Secretary at above address quoting HH/HP.

HACKNEY HOSPITAL, London, E.9. (General—841 Beds.) Applications for 6 months appointment of registered CASUALTY OFFICER AND HOUSE PHYSICIAN to Skin Department from 28th May, 1956, should be sent by 5th May, 1956, to Secretary at above address, quoting HH/HP (Skin).

HACKNEY HOSPITAL, London, E.9. (General—841 Beds.) Applications from registered practitioners for the 6 months resident appointment of CASUALTY OFFICER AND E.N.T. HOUSE SURGEON (House Officer grade), should be sent immediately to Secretary, above address, quoting HH/CHO.

HAMMERSMITH HOSPITAL AND POSTGRADUATE MEDICAL SCHOOL, Ducane-road, London, W.12. Whole-time NON-RESIDENT SENIOR REGISTRAR (Radiotherapy Department) required. Post vacant 2nd August, 1956.

Applications, stating age, qualifications, experience, names of 2 referees, to Secretary, Board of Governors, by 12th May, 1956.

HAMMERSMITH, WEST LONDON AND ST. MARK'S HOSPITALS BOARD OF GOVERNORS, Ducane-road, London, W.12. Applications invited from registered medical practitioners for the following posts :—

Hammersmith Hospital and Postgraduate Medical School

8 HOUSE PHYSICIANS (general medicine) : 4 1st July, 4 1st August.

CASUALTY OFFICER (Senior House Officer grading) : 1st July.

HOUSE SURGEON (radiotherapy) : 1st July. This post offers opportunities for attending general surgical postgraduate teaching.

Hammersmith Hospital and Institute of Obstetrics and Gynæcology

HOUSE OFFICER (gynæcology) : 1st July.

HOUSE OFFICER (obstetrics) : 1st August.

Both posts recognised for M.R.C.O.G.

Hammersmith Hospital and Institute of Child Health

HOUSE PHYSICIAN (pædiatrics) : 1st July. Post recognised for D.C.H.

Hammersmith Chest Clinic, Hammersmith Hospital

HOUSE PHYSICIAN : 1st July. For duties in tuberculosis wards and the chest clinic, dealing with all types of respiratory disease.

Applications, stating age, qualifications, experience, copies of 2 recent testimonials, to Secretary, Board of Governors, by 12th May.

HOSPITAL OF ST. JOHN AND ST. ELIZABETH, 60, Grove End-road, London, N.W.8. Required, Full-time SURGICAL REGISTRAR (Male). The possession of the Diploma of Fellow of 1 of the Royal Colleges is desirable. Honorarium at the rate of £750 p.a. Appointment will be for a period of 12 months.

Further particulars may be obtained from the Secretary to whom applications, with names of 3 referees, should be sent on or before Monday, 30th April, 1956.

HOSPITAL OF ST. JOHN AND ST. ELIZABETH, 60, Grove End-road, London, N.W.8. Applications are invited from pre-registration or registered medical practitioners (Male) for the appointment of HOUSE SURGEON, to become vacant on Monday, 14th May, 1956. This post is recognised for purposes of the F.R.C.S.(Eng.). Appointment will be for a period of 6 months. National Health Service salary.

Applications should reach the Secretary on or before Monday, 30th April, 1956, together with copies of 3 recent testimonials.

HOSPITALS FOR DISEASES OF THE CHEST. Applications invited for post of SENIOR SURGICAL REGISTRAR (whole-time). The appointment is for 1 year with eligibility for reappointment and will involve duties within the Group. Candidates must hold the Diploma of F.R.C.S.

Applications, stating age, qualifications with dates, nationality and appointments held, together with copies of testimonials, by 5th May, 1956, to—

KENNETH A. F. MILES, Secretary to the Board.

Brompton Hospital, London, S.W.3.

LAMBETH HOSPITAL, Brook-drive, S.E.11. Applications are invited from pre-registration and registered medical practitioners for the position of RESIDENT HOUSE SURGEON vacant on 5th June, 1956. The successful candidate will be required to carry out a fortnight's Locum duty starting on 22nd May, 1956.

Application forms from the Physician-Superintendent at the Hospital.

LONDON CHEST HOSPITAL. Hospitals for Diseases OF THE CHEST. A vacancy occurs for RESIDENT SURGICAL REGISTRAR at the Hospital's Country Branch, near Letchworth. There are 207 Beds, mainly surgical, and candidates should be experienced in thoracic surgery. Appointment for 6 months, with the prospect of renewal.

Applications, stating age, qualifications with dates, and previous appointments held, with copies of 3 testimonials, should be forwarded at once to the House Governor, London Chest Hospital, E.2.

NELSON HOSPITAL, Kingston-road, Merton, S.W.20. RESIDENT HOUSE PHYSICIAN AND ANÆSTHETIST (Senior House Officer grade), vacant end April.

Applications, stating age, experience and qualifications, with copies of testimonials and the name of 1 referee, should be sent to the Group Secretary, St. Helier Hospital, Carshalton, Surrey.

NORTH MIDDLESEX HOSPITAL, Edmonton, N.18. SENIOR HOUSE OFFICER in Surgery (resident) required for 7th June. General surgery, trauma and orthopædics. Post recognised for F.R.C.S.

Applications, stating age, nationality, qualifications (Primary F.R.C.S. desirable), experience, with copies of recent testimonials or names of 2 referees, to Secretary of Hospital by 7th May, 1956.

PRINCE OF WALES'S GENERAL HOSPITAL. (248 Beds.) Applications are invited from qualified medical practitioners for appointment as RESIDENT JUNIOR HOUSE SURGEON for Casualty (pre-registration first or second post) for a period of 6 months, vacant 1st June, 1956.

Application form from Secretary, Tottenham Group Hospital Management Committee (Group 4), The Green, N.15, to be returned by 19th May, 1956.

QUEEN CHARLOTTE'S AND CHELSEA HOSPITALS. SENIOR REGISTRAR (full-time) for duties at both hospitals. Candidates must have the M.R.C.O.G.

Applications, with the names of 3 referees, to the Secretary, 339, Goldhawk-road, W.6, by 12th May, 1956.

QUEEN MARY'S HOSPITAL FOR THE EAST END, Stratford, London, E.15. HOUSE SURGEON (pre-registration) for 6 months commencing as soon as possible.

Applications, with copies of recent testimonials, to Group Secretary, West Ham Group Hospital Management Committee, Stratford, E.15, by 1st May.

ROYAL FREE HOSPITAL. Applications are invited from registered medical practitioners for the post of SENIOR CASUALTY OFFICER at the Royal Free Hospital. The appointment is full-time resident, for 6 months. Duties to commence 1st July, 1956. Salary and conditions of service in accordance with those laid down by the Ministry of Health for Senior House Officers.

Application forms may be obtained from the Secretary, The Royal Free Hospital, Gray's Inn-road, W.C.1, to whom they should be returned not later than 12th May, 1956.

ROYAL MARSDEN HOSPITAL, Fulham-road, London, S.W.3. Applications are invited from registered medical practitioners for the post of HOUSE SURGEON (resident) to commence duty on 5th June, 1956. Salary £525 p.a. The post is tenable for 6 months.

Forms of application are obtainable from the House Governor, to whom applications, together with copies of 3 recent testimonials, should be sent not later than 9th May, 1956.

ROYAL NATIONAL ORTHOPÆDIC HOSPITAL, 234, Great Portland-street, London, W.1. Applications are invited for the appointment of CLINICAL ASSISTANT (whole-time). The post is graded as Senior House Officer status and will include assisting in outpatient and inpatient work. The work is that of a Junior Registrar and provides wide experience in orthopædics. The appointment to commence 1st July.

Applications to be received by 16th May. Forms of application can be obtained from the House Governor, 234, Great Portland-street, London, W.1.

ROYAL NORTHERN HOSPITAL, Holloway, London, N.7. (279 Beds.) NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. CASUALTY REGISTRAR (resident) required at the above Hospital. Experience in practical operative surgery an advantage. Recognised post for F.R.C.S. The Registrar appointed would be expected to deputise for the Resident Surgical Officer. Candidates may visit the Hospital by direct appointment.

Application forms obtainable from, and returnable to, the Secretary, Royal Northern Hospital, N.7, by 8th May, 1956.

SOUTH LODGE HOSPITAL, World's End-lane, N.21. RESIDENT HOUSE OFFICER required (first, second, or third post—not pre-registration). General duties as directed by the Medical Superintendent. Vacant 1st May, 1956.

Applications, with names and addresses of 2 referees, to the Group Secretary, Enfield Group Hospital Management Committee, Chase Farm Hospital, The Ridgeway, Enfield, Middlesex.

SOUTH LONDON HOSPITAL FOR WOMEN, Clapham Common, S.W.4. Applications are invited from pre-registration and registered Female medical practitioners for the appointment of GYNÆCOLOGICAL HOUSE SURGEON at the above Hospital, vacant 20th May, 1956, for 6 months. Recognised for the M.R.C.O.G.

Application forms from the Secretary.

SOUTH LONDON HOSPITAL FOR WOMEN, Clapham Common, S.W.4. Locum HOUSE SURGEON (Female) required at the above Hospital as soon as possible.

Applications to the Secretary.

ST. ANN'S GENERAL HOSPITAL, N.15. Applications are invited from registered medical practitioners for the appointment of RESIDENT HOUSE SURGEON (third post) to above Hospital, for a period of 6 months from 20th May, 1956.

Application form from Secretary, Tottenham Group Hospital Management Committee, The Green, N.15, to be returned by 5th May, 1956.

ST. ANN'S GENERAL HOSPITAL, N.15. Applications are invited from registered medical practitioners for the appointment of RESIDENT HOUSE SURGEON (Senior House Officer) to above Hospital for a period of 6 months from 14th June, 1956.

Application form from Secretary, Tottenham Group Hospital Management Committee, The Green, N.15, to be returned by 19th May, 1956.

ST. JOHN'S HOSPITAL FOR DISEASES OF THE SKIN, Lisle-street, Leicester-square, London, W.C.2. Applications are invited for the post of Whole-time REGISTRAR in the Department of Pathology. Candidates should be specially interested in histopathology of the skin. Previous experience in pathology desirable but not essential.

Applications, stating age, nationality, qualifications, and experience, with names of 3 referees, to the Secretary to the Board of Governors by 12th May, 1956.

ST. MARY'S HOSPITAL AND NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. (PADDINGTON GENERAL HOSPITAL.) Applications are invited for the post of Part-time REGISTRAR to the E.N.T. Departments. The successful candidate will be required to undertake, as soon as possible :—

2 notional half-days per week (Monday and Thursday mornings) at St. Mary's, and

3 notional half-days per week (Tuesday and Friday mornings and Friday afternoons) at Paddington General Hospital.

Applications, stating nationality, date of birth, permanent address, qualifications with dates, details and National Health Service gradings of previous and present appointments, together with the names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, St Mary's Hospital, W.2, not later than 9th May, 1956.

ST. MARY'S HOSPITAL, W.2. Applications are invited from suitably qualified Male candidates for the post of Whole-time REGISTRAR in the Venereal Diseases Department. The appointment is for a first period of 12 months as from a date to be arranged, the holder being eligible for re-election.

Applications, stating nationality, date of birth, qualifications, details of experience, together with dates and National Health Service gradings of previous and present appointments and names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, not later than 8th May, 1956.

ST. MARY'S HOSPITAL, W.2. Applications are invited for the post of REGISTRAR to the Pædiatric Department at St. Mary's Hospital. Previous experience in pædiatrics is necessary ; preference will be given to candidates holding the M.R.C.P. The successful candidate will be required to undertake duties in the Pædiatric Unit at St. Mary's Hospital as well as at the Constituent Children's Hospitals. The appointment will be for a first period of 12 months, with effect from 1st July, 1956, the holder being eligible for reappointment ; remuneration to be at Registrar rates. The successful applicant may be eligible to participate in an exchange scheme with the Children's Medical Centre, Boston (Harvard University).

Applications, stating nationality, date of birth, permanent address, qualifications with dates, details and National Health Service gradings of previous and present appointments, together with the names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, not later than 8th May, 1956.

ST. MARY'S HOSPITAL, W.2. Applications are invited for the post of RESIDENT HOUSE PHYSICIAN to the Neurological, Dermatological and Venereological Departments, for which either pre-registration interns seeking their second House Officer appointment, or post-registration candidates are eligible to apply. The appointment is for a period of 6 months with effect from 1st June, 1956.

Applications, stating nationality, date of birth, permanent address, qualifications with dates, details and National Health Service gradings of previous and present appointments, together with the names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, by 5th May, 1956.

ST. MARY'S HOSPITAL, W.2. Diagnostic Radiological DEPARTMENT. Applications are invited for a "POST-GRADUATE TRAINEESHIP" from persons intending to take the D.M.R.D. Course in London, October, e.g. 1956–1958. The possession of a higher qualification would be advantageous. The successful candidate will be required to take up his duties on 1st October, 1956. The appointment will be for 1 year, renewable for a second year, and will be remunerated at Senior House Officer rates.

Applications, stating nationality, date of birth, permanent address, qualifications with dates, details and National Health Service gradings of previous and present appointments, together with the names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, not later than 19th May, 1956.

ST. MARY'S HOSPITAL FOR WOMEN AND CHILDREN, Upper-road, Plaistow, E.13. HOUSE SURGEON (pre-registration) to commence immediately.

Apply to Group Secretary, West Ham Group Hospital Management Committee, Stratford, London, E.15.

WEST LONDON HOSPITAL, Hammersmith-road, W.6. 2 HOUSE PHYSICIANS (general medicine) required end June. Pre-registration candidates considered.

Applications, stating age, qualifications, experience, copies of 2 recent testimonials, to Secretary by 12th May.

WEST LONDON HOSPITAL, Hammersmith-road, W.6. Whole-time NON-RESIDENT REGISTRAR (biochemistry) required 1st July.

Applications, stating age, qualifications, experience, names of 2 referees, to Secretary, Board of Governors, Hammersmith, West London and St. Mark's Hospitals, Ducane-road, W.12, by 12th May.

ASHTON, HYDE AND GLOSSOP HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER required to assist Consultant Geriatrician in a developing unit which serves the catchment area of the Hospital Management Committee, with main duties at Ashton-under-Lyne General Hospital. There is a full scope for the study of clinical medicine and the post is suitable for a young Physician wishing to work for higher qualifications or interested in social medicine and rehabilitation. Salary £745 p.a.

Applications, together with 2 references, to the Group Secretary, General Hospital, Ashton-under-Lyne, Lancs.

ASHFORD HOSPITAL, Ashford, Middlesex. Required, RESIDENT HOUSE SURGEON (Male) for Traumatic and Orthopædic Unit. Preference given to pre-registration candidates.

Applications, stating age, qualifications and experience with copies of up to 3 recent testimonials, to Medical Director of Hospital immediately.

BEBINGTON, CHESHIRE. CLATTERBRIDGE HOSPITAL. (783 Beds.) CENTRAL WIRRAL GROUP. JUNIOR HOSPITAL MEDICAL OFFICER (casualty/orthopædics), resident, required immediately at the above Hospital. Salary in accordance with current terms and conditions of service, i.e., £775–£50–£1075 p.a., less £150 p.a. for residence.

Application forms obtainable from Hospital Secretary to be returned as soon as possible.

BEDFORD GENERAL HOSPITAL. (437 Beds.) Resident HOUSE SURGEON (gynæcology and obstetrics) required mid-May. Pre-registration post and recognised for D.Obst.R.C.O.G. The Unit comprises 26 gynæcological and 61 obstetric beds and a busy Outpatient Department.

Applications, stating age, qualifications, experience, copies of 2 recent testimonials, to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford, by 5th May, 1956.

BEDFORD GENERAL HOSPITAL. (437 Beds.) 2 Pre-registration HOUSE SURGEONS required (1 immediately and 1 mid-May). The appointments offer exceptional opportunities for general experience in busy acute surgical units.

Detailed applications, with copies of 2 recent testimonials, to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford.

BEDFORD GENERAL HOSPITAL. (437 Beds.) 2 resident Pre-registration HOUSE PHYSICIANS required approximately end May.

Applications, stating age, qualifications, experience, copies of 2 recent testimonials, to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford.

BEVERLEY, YORKSHIRE. WESTWOOD HOSPITAL. (229 Beds.) ORTHOPÆDIC HOUSE SURGEON (first, second, or third post). Married accommodation available. Offers good opportunity for general experience in busy acute general hospital. Approved pre-registration post. Fully qualified practitioners may apply. Recognised for F.R.C.S. Vacant mid-May.

Apply to Group Secretary.

BEVERLEY, YORKSHIRE. WESTWOOD HOSPITAL. ASSISTANT PATHOLOGIST (Senior House Officer grade) required in Area Laboratory with attendance at Branch Laboratory, Driffield. Offers experience all branches of pathology. Salary £745.

Detailed applications to Group Secretary.

BEXHILL HOSPITAL, Bexhill-on-Sea. (62 Beds.) House SURGEON required. Pre-registration post vacant now. National scale of salary.

Apply to Hospital Administrator.

BIRMINGHAM REGIONAL HOSPITAL BOARD.

(1) **Stoke-on-Trent Group, Princes-road, Stoke-on-Trent**

(*a*) RESIDENT MEDICAL REGISTRAR for City General Hospital (845 Beds). Higher qualification desirable but not essential. Duties in acute Medical Unit (150 Beds) and large Outpatient Department. Facilities for research, particularly in cardiology and respiratory diseases.

(*b*) REGISTRAR (pathology), for City General Hospital (845 Beds). Resident. Recognised for Dip.Path. Experience in all branches of clinical pathology available.

(2) **West Bromwich Group, Edward-street, West Bromwich**

REGISTRAR (general medicine), for Hallam Hospital (454 Beds). Resident. Experience specialty essential. Higher qualification desirable.

Application forms from the Group Secretaries, to be returned before 7th May, 1956.

BIRMINGHAM. MARSTON GREEN MATERNITY HOSPITAL, Berwicks-lane, MARSTON GREEN, near BIRMINGHAM. RESIDENT SENIOR HOUSE OFFICER in Pædiatrics required for 6 months or 1 year. (The latter to be recognised for D.C.H.) Duties in Premature Baby Unit (12 Cots), in Neonatal Department at above Hospital (121 Beds) ; and in Neonatal and Children's Department at neighbouring hospitals. Previous pædiatric or obstetric experience desirable.

Detailed applications to J. PRESTON, Group Secretary. Dudley Road Hospital, Birmingham, 18.

BIRMINGHAM. MONYHULL HALL HOSPITAL, Kings HEATH, BIRMINGHAM, 14. JUNIOR HOSPITAL MEDICAL OFFICER (resident) required at this Hospital of 1210 Beds, providing accommodation for high grade mental defectives and E.S.N. children. Recognised for D.P.M.

Applications to Medical Superintendent.

BIRMINGHAM ACCIDENT HOSPITAL. (215 Beds and 8 House Surgeons.) HOUSE SURGEON (resident), vacant at end of April. Recognised for purpose of casualty by R.C.S. (Eng.). Teaching programme by Consultant staff. Appointment for 6 months, some of which may be spent, at applicant's request, in 42-Bedded Medical Research Council's Burns Unit.

Apply to Administrator, giving names of 2 referees.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. GENERAL HOSPITAL. Applications are invited for the post of ASSISTANT RESIDENT MEDICAL OFFICER (Senior House Officer grade). The appointment, vacant 1st August, is tenable for 1 year. Candidates must be registered medical practitioners and have held a resident appointment.

Forms of application may be obtained from, and should be returned by 5th May, 1956, to the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Edgbaston, Birmingham, 15.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. THE CHILDREN'S HOSPITAL, Ladywood-road, BIRMINGHAM, 16. Applications are invited for the post of NON-RESIDENT MEDICAL REGISTRAR, to commence duty on 1st July, 1956. Preference given to applicants with M.R.C.P.

Forms of application available from the House Governor and should be returned to him not later than 12th May, 1956.

G. A. PHALP, Secretary to the Board of Governors.

BIRMINGHAM, 18. DUDLEY ROAD HOSPITAL. (780 Beds.) SENIOR HOUSE OFFICER (Casualty Department) required (40,000 attendances per year). Resident or non-resident. Recognised for F.R.C.S. Tenable for 6–12 months. Vacant 12th June, 1956.

Detailed applications, with copies of 2 recent testimonials, to Group Secretary.

BIRMINGHAM, 18. DUDLEY ROAD HOSPITAL. (780 Beds.) HOUSE PHYSICIAN (general medicine) required. Recognised for pre-registration. Vacant 1st July, 1956. Responsible for approximately 80 male and female medical beds. Unit under control of 2 Consultant Physicians.

Detailed applications, with copies of 2 recent testimonials, to Group Secretary.

BIRMINGHAM. SOLIHULL HOSPITAL, Lode-lane, SOLIHULL. HOUSE SURGEON (pre-registration), general surgery. Post vacant.

Applications, stating age, qualifications and names for reference, to Medical Superintendent.

BLACKPOOL. VICTORIA HOSPITAL. (Acute General —348 Beds.) BLACKPOOL AND FYLDE HOSPITAL MANAGEMENT COMMITTEE. CLINICAL ASSISTANT (E.N.T. Department). 5 sessions per week. Salary at the rate of £875 p.a. Eminently suitable post for practitioner studying for D.L.O.

Applications, stating age, experience, and giving names and addresses of 2 referees, should be addressed to the Hospital Secretary.

BRIGHTON GENERAL HOSPITAL. House Surgeon (recognised for F.R.C.S.), vacant 17th June, 1956. The post is recognised as a pre-registration appointment.

Applications, stating age, qualifications, experience, and giving the names of 2 referees, should be sent to the Physician-Superintendent, Brighton General Hospital, Elm-grove, Brighton, 7.

BRIGHTON GENERAL HOSPITAL. House Surgeon (orthopædics). This post is recognised as a pre-registration appointment.

Applications, stating age, qualifications, and experience, together with copies of recent testimonials, should be sent to the Physician-Superintendent, Brighton General Hospital, Elm-grove, Brighton.

BRIGHTON GENERAL HOSPITAL. Casualty/Medical OFFICER (for casualty and general duties), House Officer grade.

Applications, stating age, qualifications, and experience, together with copies of recent testimonials, should be sent to the Physician-Superintendent, Brighton General Hospital, Elm-grove, Brighton, as soon as possible.

BRIGHTON. NEW SUSSEX HOSPITAL FOR WOMEN, Windlesham-road, BRIGHTON. HOUSE PHYSICIAN (Female), 6 months. Includes duties in Gynæcological Department. Open to pre-registration candidates.

Applications, stating age, nationality, qualifications and experience, with copies of 3 testimonials and/or names of referees, to Administrative Officer before 4th May, 1956.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL. (312 Beds.) HOUSE SURGEON required mid-May. Recognised for pre-registration and F.R.C.S.

Applications, stating usual particulars, and naming 2 referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7.

BRIGHTON. ROYAL ALEXANDRA HOSPITAL FOR SICK CHILDREN, Dyke-road, BRIGHTON. (129 Beds.) SENIOR HOUSE OFFICER (12 months), HOUSE SURGEON (6 months), HOUSE PHYSICIAN (6 months). Candidates for the senior post should have had experience in pædiatrics. All posts recognised for D.C.H.; that of House Surgeon is open to pre-registration candidates.

Applications, stating age, nationality, qualifications and experience, with copies of 3 testimonials and/or names of referees, to Administrative Officer before 4th May, 1956.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL, Shelley-road, BOSCOMBE. BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of 2 HOUSE PHYSICIANS. The posts which become vacant on 31st May and 4th June are recognised for pre-registration purposes.

Applications to the Hospital Secretary at the Hospital.

BRISTOL. COSSHAM AND FRENCHAY HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON in General Surgery required at Cossham Memorial Hospital, Kingswood, Bristol, now until 31st July, 1956. 88 Beds acute medicine and surgery. Recognised pre-registration post but fully registered practitioners considered.

Apply to Group Secretary, Frenchay Hospital, Bristol, quoting qualifications, experience and names of 2 referees.

BRISTOL MENTAL HOSPITAL MANAGEMENT COMMITTEE. Applications invited from registered medical practitioners for JUNIOR HOSPITAL MEDICAL OFFICER post at Fishponds Hospital. Salary and conditions according to Health Service scale £775–£1075. Post offers wide scope in psychiatry and its special branches including Neurosis Centre and Day Hospital. Holder will have opportunity of studying and gaining experience for Diploma in Psychological Medicine. Modern house available. Board-residence can be provided for single officer.

Applications, with names of 3 referees, should be sent to Medical Superintendent, Barrow Hospital, Barrow Gurney, near Bristol.

BRISTOL (near). HAM GREEN HOSPITAL, Pill, BRISTOL. Applications are invited for the post of SENIOR HOUSE OFFICER in the tuberculosis wards (188 Beds) of the above Hospital. The Hospital is fully equipped for the modern treatment of pulmonary tuberculosis including regular major thoracic surgery. Appointment for 1 year renewable.

Apply Secretary, Ham Green Hospital, Pill, near Bristol.

BURY AND ROSSENDALE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER in Pædiatrics. The post is based on Bury General Hospital, but will include duties at other hospitals in the Group. Post recognised for D.C.H.

Apply, stating age, qualifications, experience and names of 2 referees, to H. WILKINSON, Group Secretary.

Bury General Hospital, Bury, Lancs.

BURY AND ROSSENDALE HOSPITAL MANAGEMENT COMMITTEE. BURY GENERAL HOSPITAL. SENIOR HOUSE OFFICER (surgical) at the above Hospital. Salary and conditions of service in accordance with national rules. Post recognised for Fellowship.

Applications should be made to—

H. WILKINSON, Esq., Group Secretary.

Bury General Hospital, Bury, Lancs.

BURY AND ROSSENDALE HOSPITAL MANAGEMENT COMMITTEE. FAIRFIELD GENERAL HOSPITAL. SENIOR HOUSE OFFICER (gynæcology and obstetrics). Applications are invited for the above post.

Apply, stating age, qualifications and experience, together with names of 2 referees, to H. WILKINSON, Group Secretary.

Bury General Hospital, Bury, Lancs.

CAMBRIDGE. ADDENBROOKE'S HOSPITAL. Medical REGISTRAR (non-resident) for 1 year in first instance, vacant June, renewable for second year.

Apply, with full particulars and names of 3 referees, to Secretary by 12th May.

CARDIFF. PRINCE OF WALES ORTHOPÆDIC HOSPITAL, RHYDLAFAR, CARDIFF. SENIOR HOUSE OFFICER required. Regional Orthopædic Centre for South Wales area of 220 Beds increasing to 290 and branch of 70 Beds. Outpatients clinic in Cardiff. Single accommodation at Hospital at Rhydlafar.

Form of application from Group Secretary, Cardiff Hospital Management Committee, 44, Cathedral-road, Cardiff.

CARDIFF. ROYAL HAMADRYAD GENERAL AND SEAMEN'S HOSPITAL. RESIDENT SENIOR HOUSE OFFICER (surgical) required at above Hospital. Post covers 44 Beds—genito-urinary, general surgery and outpatients. Department under care of Consultants from United Cardiff Hospitals.

Form of application from Group Secretary, Cardiff Hospital Management Committee, 44, Cathedral-road, Cardiff.

CHELMSFORD. ST. JOHN'S HOSPITAL. House SURGEON (pre-registration first, second, or third post). Duties commence 1st June, 1956. The Hospital deals with a large number of routine and emergency cases. The post is recognised for training for the F.R.C.S.

Applications stating age, nationality, qualifications and experience, together with copies of recent testimonials, should be received not later than 8th May, 1956, by the Secretary, Chelmsford Group Hospital, Management Committee, Chelmsford and Essex Hospital, London-road, Chelmsford.

CHELMSFORD. ST. JOHN'S HOSPITAL. House PHYSICIAN (pre-registration, first, second, or third appointment), Male or Female, to commence as soon as possible.

Applications, stating age, nationality, qualifications, and experience, together with recent testimonials, to the Secretary, Group Hospital Management Committee, Chelmsford and Essex Hospital, London-road, Chelmsford.

CHELMSFORD AND ESSEX HOSPITAL. (162 Beds.) Applications are invited for the post of RESIDENT HOUSE SURGEON (pre-registration post). Post vacant now and offers good surgical experience and is recognised for the F.R.C.S.

Applications, together with 2 recent testimonials, to the Secretary, Chelmsford Hospital Management Committee, London-road, Chelmsford.

CHELTENHAM GENERAL AND EYE HOSPITAL. (170 Beds.) JUNIOR HOSPITAL MEDICAL OFFICER (casualty) required.

Applications, giving details of qualifications and experience, and names of 3 referees, to be sent to the Group Secretary, General Hospital, Sandford-road, Cheltenham.

CHESTERFIELD ROYAL HOSPITAL. (279 Beds.) RESIDENT HOUSE SURGEON required immediately at above Hospital. Post recognised for Pre-registration Service and F.R.C.S. examinations. National salary and conditions.

Apply M. H. BOONE, Secretary, Chesterfield Hospital Management Committee.

CHICHESTER. ROYAL WEST SUSSEX HOSPITAL. (202 acute beds.) RESIDENT HOUSE SURGEON required for 6 months appointment. National salary scale for first, second, or third posts. Post approved for pre-registration practitioners. Also recognised for F.R.C.S. 7 residents, including Resident Surgical Officer and 3 House Surgeons. Vacant 29th April.

Apply to Senior Administrative Officer.

CHESTER-LE-STREET. GENERAL HOSPITAL. (204 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (general surgery). Post vacant now. Resident.

Apply, with particulars of age, experience and names of 2 referees, to Group Secretary, Dryburn Hospital, Durham.

CROYDON. MAYDAY HOSPITAL. (611 Beds.) House SURGEON (pre-registration) for period of 6 months commencing 5th June, 1956. Post recognised for F.R.C.S. Preference given to candidates who have held previous House Officer post.

Application forms obtainable from GEORGE A. PAINES, Group Secretary, Hospital Management Committee, General Hospital, London-road, Croydon, to be returned immediately.

CROYDON GENERAL HOSPITAL. (200 Beds.) House SURGEON (pre-registration) required as from 11th May, 1956. Post recognised for F.R.C.S.

Application forms obtainable from GEORGE A. PAINES, Group Secretary, Hospital Management Committee, General Hospital, London-road, Croydon, to be returned immediately.

CROYDON EYE UNIT. Applications invited for post of OPHTHALMIC HOUSE SURGEON to the Croydon Eye Unit; Inpatient and Outpatient Departments. Post vacant now.

Application form obtainable from GEORGE A. PAINES, Group Secretary, General Hospital, London-road, Croydon.

CARMARTHEN. WEST WALES GENERAL HOSPITAL. (188 Beds.) WEST WALES HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (orthopædic and traumatic surgery) which is now vacant. Salary and conditions of service as laid down by Ministry of Health.

Applications, stating age, qualifications, experience, nationality with names and addresses of 3 referees, to the Group Secretary, West Wales Hospital Management Committee, Glangwili, Carmarthen.

CLACTON AND DISTRICT HOSPITAL, Clacton-on-Sea. (58 Beds.) Applications invited for post of REGISTRAR (Resident Surgical Officer). Required temporarily, mid-May–mid-September.

Applications, with copies of 3 testimonials, to the Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

DERBY. DERWENT HOSPITAL. (187 Beds.) Sheffield REGIONAL HOSPITAL BOARD. Whole-time REGISTRAR (chest and infectious diseases) required. Private quarters available. A Consultant Thoracic Surgeon attends this Hospital each week. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 7th May, 1956, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

DERBY. DERBYSHIRE ROYAL INFIRMARY. Senior HOUSE OFFICER (E.N.T.). Recognised for F.R.C.S. Post now vacant. Duties include attendance at 2 other hospitals within the Group. Canvassing disqualifies.

Applications, with copies of 2 recent testimonials, to Secretary.

DONCASTER ROYAL INFIRMARY. (330 Beds. Recognised for training for F.R.C.S. examination.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time REGISTRAR (orthopædics) required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 7th May, 1956, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

DORKING GENERAL HOSPITAL, Horsham-road, DORKING. Applications are invited for the post of SENIOR HOUSE OFFICER (general surgery, orthopædics and E.N.T.), vacant middle of May, 1956.

Apply, with copies of 2 recent testimonials, to Medical Superintendent.

DRIFFIELD, YORKSHIRE. EAST RIDING GENERAL HOSPITAL. (247 Beds.) HOUSE PHYSICIAN (first, second, or third post), vacant now. Approved pre-registration post. Fully qualified practitioners may apply. Duties to include acute and chronic sick and casualties. Good general experience for first house appointment.

Apply Group Secretary, Westwood Hospital, Beverley, Yorkshire.

DRIFFIELD, YORKSHIRE. NORTHFIELD SANATORIUM. (78 Beds.) SENIOR HOUSE PHYSICIAN, vacant now, offers experience all branches of tuberculosis within Group, including surgery, M.M.R., and clinics. Time for study. Expatients welcome. £165 for full residence.

Applications to Group Secretary, Westwood Hospital, Beverley, Yorkshire.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. SENIOR MEDICAL REGISTRAR, United Norwich Hospitals. Main hospital Norfolk and Norwich (441 Beds). Trainee post. Higher qualification desirable.

Applications, stating age, experience, and the names of 3 referees, to Board Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge by 7th May, 1956. Candidates invited to visit hospitals by direct arrangement with Hospital Management Committee Secretary, Norfolk and Norwich Hospital.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. (1) SURGICAL REGISTRAR, Ipswich and East Suffolk Hospital. Post recognised for F.R.C.S. Appointment for 1 year, renewable for second year. Candidates invited to visit hospitals by direct arrangement with Hospital Management Committee Secretary, Ipswich and East Suffolk Hospital (Anglesea Road Wing), Ipswich.

(2) REGISTRAR in Plastic Surgery, Regional Plastic Surgery and Burns Unit (28 Beds), West Norwich Hospital (Norfolk and Norwich Hospital Group). Post offers wide experience and training. Appointment for 1 year, renewable for second year. Candidates invited to visit hospitals by direct arrangement with Hospital Management Committee Secretary, Norfolk and Norwich Hospital, Norwich.

Applications, stating age, experience and the names of 3 referees, to the Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 14th May, 1956.

EDGWARE GENERAL HOSPITAL. (715 Beds.) Resident SENIOR HOUSE OFFICER in Pathology required at above Hospital. Salary £745 p.a. Deduction of £155 p.a. for board, lodging, &c.

Applications, stating age, qualifications and experience, together with names and addresses of 2 referees, to Group Secretary, Edgware General Hospital, Edgware, Middlesex, by 9th May, 1956.

EDGWARE GENERAL HOSPITAL, Edgware, Middlesex. RESIDENT PÆDIATRIC HOUSE PHYSICIAN for above Hospital. Post vacant 1st June, 1956. 6 months appointment. Post recognised for pre-registration and D.C.H. purposes.

Applications, stating age, qualifications, experience, and enclosing copies of up to 3 testimonials, to Medical Director of Hospital by 12th May, 1956.

ELLESMERE PORT HOSPITAL. Applications are invited for the post of RESIDENT MEDICAL OFFICER (Junior Hospital Medical Officer). A furnished semi-detached house is available at a reasonable rental for married practitioner.

Applications, giving full details together with the names and addresses of 2 referees, should be forwarded to the Group Secretary, XIII Chester and District Hospital Management Committee, 5, King's-buildings, Chester.

ENFIELD, MIDDLESEX. WAR MEMORIAL HOSPITAL, CHASE SIDE. RESIDENT SENIOR HOUSE OFFICER required for general medical and surgical duties in this Acute General Hospital of 61 Beds, vacant now. 12 months appointment. Deduction of £160 p.a. for residential emoluments.

Applications, with names and addresses of 2 referees, to the Group Secretary, Enfield Group Hospital Management Committee, Chase Farm Hospital, The Ridgeway, Enfield, Middlesex.

ENFIELD, MIDDLESEX. CHASE FARM HOSPITAL. RESIDENT HOUSE SURGEON required (third post), vacant 23rd June, 1956. Post provides experience and duties in both surgery and orthopædics. 6 months appointment. Recognised for F.R.C.S. by the Royal College of Surgeons.

Applications, with names and addresses of 2 referees, to the Group Secretary, Enfield Group Hospital Management Committee.

EPSOM DISTRICT HOSPITAL, Dorking-road, Epsom, SURREY. RESIDENT HOUSE SURGEON required 11th June. Pre-registration post. Recognised for F.R.C.S.

Applications, stating age, qualifications and experience with copies of 2 recent testimonials, should be sent as soon as possible to Group Secretary at above address.

EPSOM DISTRICT HOSPITAL, Dorking-road, Epsom, SURREY. RESIDENT HOUSE PHYSICIAN required 6th June. Pre-registration post.

Applications, stating age, qualifications and experience with copies of 2 recent testimonials, should be sent as soon as possible to Group Secretary at above Hospital.

GAINSBOROUGH. JOHN COUPLAND HOSPITAL. (40 Beds.) Applications are invited for the post of RESIDENT MEDICAL OFFICER. The Hospital has a number of both medical and surgical beds. Salary is in accordance with Junior Hospital Medical Officer grade of the terms laid down for hospital medical and dental staffs. Married quarters are available.

Applications, giving full particulars, should be forwarded as soon as possible to—

R. W. HOWICK, Group Secretary,
Lincoln No. 1 Hospital Management Committee.
County Hospital, Lincoln.

GLASGOW, S.W.1. SOUTHERN GENERAL HOSPITAL. SENIOR HOUSE OFFICER in Surgery.

Write to Secretary, Board of Management for Glasgow South-Western Hospitals, 1301, Govan-road, Glasgow, S.W.1, by 5th May, 1956, naming 2 referees.

GUILDFORD. ROYAL SURREY COUNTY HOSPITAL. (233 Beds.) RESIDENT HOUSE SURGEON required for general surgery. Post is vacant on 18th May and tenable for 6 months. It is approved for pre-registration practitioners and recognised for the F.R.C.S. examination.

Applications, with copies of 3 testimonials, should be sent to the Hospital Secretary as soon as possible.

GUILDFORD. ROYAL SURREY COUNTY HOSPITAL. (233 Beds.) RESIDENT HOUSE PHYSICIAN required from 1st June. Post is tenable for 6 months and is recognised for pre-registration candidates.

Applications, with copies of 3 testimonials, should be sent to the Hospital Secretary as soon as possible.

HASTINGS. ROYAL EAST SUSSEX HOSPITAL. (150 Beds.) HOUSE SURGEON required. Pre-registration post, vacant now. National scale of salary.

Apply to Hospital Administrator.

HEMEL HEMPSTEAD, HERTFORDSHIRE. WEST HERTS HOSPITAL. CASUALTY OFFICER (Junior Hospital Medical Officer) required.

Applications, stating 2 names for reference, should be sent to the Hospital Secretary.

HEMEL HEMPSTEAD. WEST HERTS AND ST. PAUL'S HOSPITALS. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. OBSTETRICAL AND GYNÆCOLOGICAL REGISTRAR (resident) required at above Hospitals which may be visited by direct appointment. Post vacant early July.

Application form obtainable from, and returnable to, Secretary, West Herts Group Hospital Management Committee, 9, Rickmansworth-road, Watford, Herts, by not later than 10 days after the appearance of this advertisement.

HUDDERSFIELD ROYAL INFIRMARY. (312 Beds.) HOUSE SURGEON (Female) required to commence duty immediately. The post is recognised as a pre-registration appointment and for the F.R.C.S. Salary in accordance with national scale.

Applications, together with copies of 3 recent testimonials, to be addressed to the undersigned as soon as possible.

H. J. JOHNSON, Secretary,
Huddersfield Hospital Management Committee.
The Royal Infirmary, Huddersfield.

HEREFORD. COUNTY HOSPITAL. (335 Beds.) House OFFICER (surgery) required. Hospital recognised for F.R.C.S.

Applications, with copies of 2 recent testimonials, to Medical Superintendent, County Hospital.

HERTFORD COUNTY HOSPITAL. (171 Beds. Hospital situated 21 miles from London.) Applications are invited for appointment of RESIDENT HOUSE PHYSICIAN (Male or Female), second post held. Recognised pre-registration post. 6 months appointment. Preference given to applicants who have held resident surgical or medical posts in general hospital. Duties to commence 19th June, 1956.

Applications to Group Secretary, Hertford Hospital Management Committee, County Hospital, Hertford, Herts.

HENLEY-ON-THAMES, OXFORDSHIRE. PEPPARD CHEST HOSPITAL. (236 Beds.) Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER. Resident accommodation available for a single applicant. Further details may be obtained from the Physician-Superintendent.

Applications, with the names of 2 referees, should be addressed to the Acting Group Secretary, Reading and District Hospital Management Committee, 3, Craven-road, Reading.

HEXHAM, NORTHUMBERLAND. WOOLEY SANA-TORIUM. JUNIOR RESIDENT MEDICAL OFFICER commencing as soon as possible. The appointment is suitable for, and preference will be given to, someone who has suffered from tuberculosis, and the grading is House Officer (pre-registration), Senior House Officer, or Junior Hospital Medical Officer, according to experience. Married accommodation, either a house or flat, is available.

Applications to Medical Superintendent.

HOVE GENERAL HOSPITAL, Sussex. (75 Beds.) Senior HOUSE OFFICER (recognised for F.R.C.S.), vacant 1st June. Duties of Resident Surgical Officer. Appointment for period of 1 year.

Applications, with full particulars of qualifications, experience, &c., with names and addresses of 2 referees, to the Administrative Officer as soon as possible.

HOUNSLOW HOSPITAL, Staines-road, Hounslow, MIDDLESEX. (General Acute—81 Beds.) Applications are invited for the appointment of RESIDENT HOUSE PHYSICIAN. Recognised pre-registration appointment. Vacant 25th June, 1956.

Applications, stating qualifications and age, together with copies of up to 3 recent testimonials, or names for reference, to the Hospital Secretary.

HOUNSLOW HOSPITAL, Staines-road, Hounslow, MIDDLESEX. (General Acute—81 Beds.) Applications are invited for the appointment of RESIDENT HOUSE SURGEON. Recognised pre-registration appointment. Vacant 20th May, 1956.

Applications, stating qualifications and age, together with copies of up to 3 recent testimonials, or names for reference, to the Hospital Secretary.

ILFORD. KING GEORGE HOSPITAL, Eastern-avenue. There will be vacancies for the following at above Hospital.

HOUSE SURGEON—31st May, 1956. First or second post pre-registration.

HOUSE SURGEON—14th June, 1956. Second post pre-registration.

The posts will be tenable for 6 months.

Applications, giving full particulars and accompanied by testimonials, should be sent to the undersigned within 7 days of the appearance of this advertisement.

H. F. HARRIS, Group Secretary, Ilford
and Barking Group Hospital Management Committee.

ILKLEY (near). MIDDLETON HOSPITAL. (430 Beds.) JUNIOR HOSPITAL MEDICAL OFFICER required for the above Hospital which provides medical and surgical treatment for all types of tuberculosis. Accommodation available for single applicants.

Applications to Medical Superintendent at the above address as soon as possible.

IPSWICH AND EAST SUFFOLK HOSPITAL. Anglesea ROAD WING. (356 Beds.) Applications are invited for the post of HOUSE SURGEON to the E.N.T. and Ophthalmic Departments, vacant on 13th June, 1956. The post is recognised for pre-registration and for the D.L.O. examination.

Applications, giving full particulars and copies of recent testimonials, to Hospital Secretary.

IPSWICH AND EAST SUFFOLK HOSPITAL. Anglesea ROAD WING. (356 Beds.) Applications are invited for the post of HOUSE SURGEON to the General Consultant Surgeon, vacant on 12th May, 1956. The post is recognised for pre-registration and for the F.R.C.S. examinations.

Applications, with copies of recent testimonials, to the Hospital Secretary.

IPSWICH AND EAST SUFFOLK HOSPITAL. Anglesea ROAD WING. (356 Beds.) Applications are invited for the post of HOUSE PHYSICIAN, vacant on 1st June, 1956. Approved pre-registration post.

Applications, stating age, nationality and experience, together with copies of 3 recent testimonials, to reach the Hospital Secretary by 7th May, 1956.

KINGSTON HOSPITAL, Wolverton-avenue, Kingston-UPON-THAMES. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified medical officers for the post of Locum SENIOR HOUSE OFFICER (orthopædic and casualty). The post is recognised in casualty for F.R.C.S. purposes and is available from 28th July, 1956, to 11th August, 1956.

Applications, stating age, qualifications and experience, with 2 recent testimonials, should reach the Physician-Superintendent of the Hospital as soon as possible.

LUTON AND DUNSTABLE HOSPITAL, Luton, Bed-FORDSHIRE. SENIOR HOUSE OFFICER (resident) in Medicine required. Post now vacant.

Applications, stating age, nationality, qualifications, and experience, together with copies of 3 recent testimonials, to be sent to the Secretary as soon as possible.

LEAMINGTON SPA. WARNEFORD GENERAL HOS-PITAL. (197 Beds.) HOUSE PHYSICIAN (pre-registration post), vacant 7th June, 1956.

Applications, with names of 2 recent referees, to be sent to Hospital Secretary.

LEEDS. THE UNITED LEEDS HOSPITALS. The GENERAL INFIRMARY AT LEEDS. REGISTRAR in Anæsthetics required for duties in the Teaching Hospital Group. Terms and conditions of service for hospital medical staff apply.

Applications, stating age, qualifications, experience with relevant dates, and giving 3 names for reference, should be forwarded to the Sub-Dean, The Medical School, Leeds, 2, not later than 12th May, 1956.

LEEDS. THE UNITED LEEDS HOSPITALS. The MATERNITY HOSPITAL AT LEEDS. SENIOR HOUSE OFFICER required for the Pædiatric Unit for a period of 1 year. Post vacant 5th July, 1956. Successful candidate will work under the direction of the Professor of Pædiatrics and Child Health and be responsible to him for the supervision and management of healthy and ailing babies in the Leeds Maternity Hospital. Previous experience of resident house posts in pædiatrics and/or obstetrics is desirable but not absolutely essential.

Applications, stating age, qualifications, previous posts with dates, and the names of 2 referees, should be sent to the Secretary to the Board, the General Infirmary at Leeds, as soon as possible.

MAIDENHEAD HOSPITAL, St. Luke's-road, Maiden-HEAD. RESIDENT SURGICAL REGISTRAR. Hospital may be visited by direct appointment.

Application forms from, and returnable to, Secretary, Windsor Group Hospital Management Committee, Alma-road, Windsor, by 11th May.

MAIDSTONE. KENT COUNTY OPHTHALMIC AND AURAL HOSPITAL. (113 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE SURGEON in the E.N.T. Department of the above Hospital. Post vacant May, 1956. There are 55 E.N.T. beds and 6 specialist operating sessions each week. Valuable experience is available, and the post is recognised for the purpose of the F.R.C.S. and the D.L.O. Salary will be £745 a year, less £150 a year for residential emoluments.

Applications immediately to the Administrative Officer, Kent County Ophthalmic and Aural Hospital, Maidstone, Kent.

MAIDSTONE. WEST KENT GENERAL HOSPITAL. (141 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE. CASUALTY OFFICER (Senior House Officer). Recognised for F.R.C.S. Salary £745 a year, less £150 a year for board and lodging. Post vacant June, 1956.

Applications to the Administrative Officer at the Hospital.

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL EYE HOSPITAL. Applications are invited for the post of SENIOR REGISTRAR at the above Hospital (attached to the University Department of Ophthalmology). Whole-time post (non-resident). Tenable for 12 months, subject to renewal. Previous experience in ophthalmology essential. The terms and conditions of service for hospital medical and dental staffs will apply.

Applications to be made as soon as possible on forms obtainable from the undersigned.

H. R. NORTH General Superintendent.

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL INFIRMARY, MANCHESTER, 13. 2 SENIOR HOUSE OFFICERS (surgical) to commence on 18th June and 1st August, 1956. Whole-time non-resident training post, tenable for 6 months, renewable for a second 6 months. Duties allotted in Orthopædic, Surgical Outpatients and General Surgical Units in rotation.

Application form obtainable from the undersigned, to be returned as soon as possible. G. H. TAYLOR, Secretary.

MANCHESTER, 20. CHRISTIE HOSPITAL AND HOLT RADIUM INSTITUTE. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (surgery) at the above Hospital.

Applications, stating age, qualifications, nationality, present post, experience, and names of 2 referees, to the Group Secretary, Withington Hospital, Manchester, 20, as soon as possible.

MANCHESTER. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (anæsthetics) with duties in the South Manchester Group. This post is recognised by the Royal College of Surgeons for the F.F.A.R.C.S. and for the D.A.

Applications, stating age, qualifications, present post, experience, and names of 2 referees, to be forwarded immediately to the Group Secretary, Withington Hospital, Manchester, 20.

MANCHESTER REGIONAL HOSPITAL BOARD. Salford HOSPITAL MANAGEMENT COMMITTEE. HOPE HOSPITAL. Applications are invited for post of REGISTRAR in Obstetrics and Gynæcology, vacant 17th June, 1956. Hospital recognised for M.R.C.O.G.

Applications, stating age, qualifications and experience, together with names of 3 referees, to be sent to Group Secretary Salford Royal Hospital, Salford, 3, before 5th May, 1956.

MANCHESTER REGIONAL HOSPITAL BOARD invites applications for the post of REGISTRAR in Pathology. The duties will be with the Stockport and Buxton Hospital Management Committee and the successful candidate will work under the direction of the Consultant Group Pathologist.

Applications, stating age, experience, and qualifications, together with copies of 2 testimonials to be addressed to the Group Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw-heath, Stockport, Cheshire.

MANCHESTER REGIONAL HOSPITAL BOARD. RESI-DENT SURGICAL REGISTRAR required mid-May for the Royal Infirmary, Blackburn, a busy acute hospital of 262 Beds. Post recognised for F.R.C.S.

Application forms available from Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

MANCHESTER REGIONAL HOSPITAL BOARD invite applications for the post of REGISTRAR in General Surgery to the Blackpool and Fylde Group of Hospitals, with main duties at Victoria Hospital, Blackpool (348 Beds). The post, which is vacant in July, is recognised under the F.R.C.S. regulations. The appointment offers an excellent opportunity for gaining practical experience in general and emergency surgery to suitable qualified candidates.

Applications, stating age, qualifications and experience, together with the names of 3 referees, should be sent to the Group Secretary, Blackpool and Fylde Hospital Management Committee, Victoria Hospital, Blackpool.

MANCHESTER, 23. WYTHENSHAWE HOSPITAL. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER (surgical) at the above Hospital. General surgery and casualty duties.

Applications, with full details, to be forwarded to the Group Secretary, Withington Hospital, Manchester, 20, immediately.

MIDDLESBROUGH. HEMLINGTON HOSPITAL. (282 Beds.) TEES-SIDE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE SURGEON. This post entails duties in connection with acute surgery, gynæcology and plastic surgery beds.

Applications, stating age, qualifications, together with names for reference, to be forwarded to the Hospital Secretary.

MID-KENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of RESIDENT ANÆSTHETIST for joint duties at the West Kent General Hospital, and the Kent County Ophthalmic and Aural Hospital, Maidstone (total beds 254). The post, which is of Senior House Officer grade, will be vacant June, 1956, and carries a salary of £745 a year, less £150 for residential emoluments. Excellent experience under Consultant Anæsthetists is available, and the post is recognised for the F.F.A.R.C.S. examination.

Applications, stating age, nationality, qualifications and experience, together with the names of 2 suitable referees, should be forwarded to the Administrative Officer, West Kent General Hospital, Maidstone.

NEWCASTLE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS. Applications are invited for the whole-time non-resident appointment of SENIOR REGISTRAR to the Department of Psychological Medicine at the Royal Victoria Infirmary under the clinical direction of the Professor of Psychological Medicine. Applicants should possess either a Diploma in Psychological Medicine or a higher qualification in general medicine, and psychiatric experience. The appointment is for 1 year in the first instance and will be subject to the terms and conditions of service of hospital medical staff in the National Health Service. The successful candidate will be expected to take up his duties on 1st July, 1956.

Applications, giving full details and the names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the appearance of this advertisement.

A. W. SANDERSON, House Governor and Secretary.
Royal Victoria Infirmary, Newcastle upon Tyne.

NEWCASTLE REGIONAL HOSPITAL BOARD. Regional BLOOD TRANSFUSION SERVICE. MEDICAL OFFICER (Junior Hospital Medical Officer grade) whole-time, for a period not exceeding 4 years. Experience in serology preferable, but not essential. Duties in the laboratory and in blood collection.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Walker Gate Hospital, Benfield-road, Newcastle upon Tyne, 6, within 14 days.

NEWCASTLE REGIONAL HOSPITAL BOARD. SEDGEFIELD HOSPITAL MANAGEMENT COMMITTEE. Locum REGISTRAR OBSTETRICIAN AND GYNÆCOLOGIST (whole-time) from 1st July, 1956. Modern self-contained unfurnished flat (5 rooms) available.

Applications, with names and addresses of 3 referees, to be forwarded to Senior Administrative Medical Officer, Walker Gate Hospital, Benfield-road, Newcastle upon Tyne, 6.

NEWCASTLE REGIONAL HOSPITAL BOARD. CLEVELAND HOSPITAL MANAGEMENT COMMITTEE. REGISTRAR PÆDIATRICIAN (whole-time) Children's Hospital, Stockton on Tees (84 Beds). Well-furnished married accommodation available.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Walker Gate Hospital, Benfield-road, Newcastle upon Tyne, 6, within 14 days.

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time GYNÆCOLOGICAL AND OBSTETRIC REGISTRAR (resident) required for duties mainly at St. Albans City Hospital (384 Beds). Hospital may be visited by direct appointment.

Application forms obtainable from, and returnable to, Secretary, Mid Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans, Herts, by 7th May, 1956.

NOTTINGHAM. CITY HOSPITAL. (811 Beds.) Applications are invited for the post of HOUSE SURGEON, vacant 15th May, 1956. Recognised for pre-registration purposes.

Applications, stating age, nationality, qualifications and experience, together with copies of not more than 3 testimonials, to be sent to the Hospital Secretary, City Hospital, Hucknall-road, Nottingham.

NOTTINGHAM. CITY HOSPITAL. (804 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (general surgery) vacant 1st June, 1956. The post is approved for the F.R.C.S. The Officer appointed will also be required to undertake certain duties in the Orthopædic Department. A deduction of £150 p.a. will be made for residential emoluments.

Applications, stating age, nationality, qualifications and experience, together with copies of not more than 3 testimonials, to be sent to the Hospital Secretary, City Hospital, Hucknall-road, Nottingham.

NOTTINGHAM GENERAL HOSPITAL. Resident HOUSE SURGEONS (2) (first or second post) required as soon as possible for 6 months.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to the Group Secretary.

OXFORD REGIONAL HOSPITAL BOARD. Registrar (whole-time) in Psychiatry at Fair Mile (Mental) Hospital, near Wallingford (Berks), and Associated Clinics. Recognised for the D.P.M. and full facilities for training are available in the Area Department. The appointment will be for 1 year and eligible for extension to a second year. There is no married accommodation.

Applications on forms obtainable from the Secretary, Registrars Committee, 43, Banbury-road, Oxford, should reach him by 14th May, 1956.

OXFORD. UNITED OXFORD HOSPITALS. Applications are invited for 2 posts of RESIDENT JUNIOR PATHOLOGIST for 6 months; 1 at the Churchill Hospital and 1 at the Radcliffe Infirmary, Oxford. The posts are graded at Senior House Officer rate £745 p.a. and are vacant early in May.

Applications, stating age, qualifications and experience, together with names of 2 referees, to the Administrator, Radcliffe Infirmary, Oxford, as soon as possible.

POOLE GENERAL HOSPITAL, Longfleet-road, Poole, DORSET. BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. 2 HOUSE SURGEONS (pre-registration) required. 1 post vacant 25th May, and second on 20th June, 1956. Posts recognised for F.R.C.S. and F.R.C.S.E.

Applications to the Hospital Secretary at the Hospital.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL.

SENIOR HOUSE OFFICER in Anæsthetics, vacant 1st July, 1956. Recognised for the D.A. and F.F.A.R.C.S. The appointment will be for a period of 12 months. South Devon and East Cornwall Hospital, Plymouth.

SENIOR HOUSE OFFICER in Surgery, vacant immediately. Recognised for the F.R.C.S. Devonport Section.

SENIOR HOUSE OFFICER in Casualty, vacant 1st July, 1956. Recognised for the F.R.C.S. The Central Casualty Department, South Devon and East Cornwall Hospital, Freedom Fields, Plymouth.

HOUSE SURGEONS (pre-registration posts), 2 vacancies 1st July, 1956. Recognised for the F.R.C.S. Freedom Fields Section.

HOUSE SURGEONS (pre-registration posts), vacancies 12th June, and 1st July, 1956. Recognised for the F.R.C.S. Greenbank Road Section.

RESIDENT DENTAL HOUSE SURGEON, vacant 8th July, 1956. This appointment is recognised by the Royal College of Surgeons as fulfilling the requirements of candidates for the Fellowship of Dental Surgery. Greenbank Road Section.

HOUSE SURGEON (pre-registration post), vacant 1st June, 1956. Recognised for the F.R.C.S. Devonport Section.

Applications, stating age, nationality, qualifications and experience, with names of 3 referees, to be sent to—

ARTHUR R. CASH, Group Secretary, Plymouth,
South Devon and East Cornwall General Hospital Group,
7, Nelson-gardens, Stoke, Plymouth.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL, Greenbank-road. SENIOR HOUSE OFFICER in Surgery, vacant immediately. Recognised for the F.R.C.S.

Applications, stating age, nationality, qualifications and experience, with names of 3 referees, to—

ARTHUR R. CASH, Group Secretary, Plymouth,
South Devon and East Cornwall General Hospital Group.
7, Nelson-gardens, Stoke, Plymouth.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL. DEPARTMENT OF OBSTETRICS AND GYNÆCOLOGY. HOUSE OFFICER in Obstetrics and Gynæcology, vacant 1st July, 1956. Recognised for the Membership of the Royal College of Obstetricians and Gynæcologists. Wide experience can be obtained in obstetrics, including antenatal and postnatal clinics.

Applications, stating age, nationality, qualifications and experience, with names of 3 referees, to be sent to—

ARTHUR R. CASH, Group Secretary, Plymouth,
South Devon and East Cornwall General Hospital Group.
7, Nelson-gardens, Stoke, Plymouth.

PLYMOUTH. SCOTT ISOLATION HOSPITAL. RESIDENT HOUSE PHYSICIAN (Male, unmarried), vacancy end of May. Recognised, pre-registration post which offers excellent experience.

Applications should be sent to the Group Secretary, Plymouth Special Hospital Management Committee, 8, Nelson-gardens, Stoke, Plymouth, Devon, as soon as possible.

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE.

Queen Alexandra Hospital (87 surgical beds)
HOUSE SURGEON (pre-registration), vacant now.
Queen Alexandra Hospital (78 medical beds)
HOUSE PHYSICIAN (pre-registration), vacant now.
Saint Mary's Hospital (130 surgical beds)
HOUSE SURGEON (pre-registration), vacant 9th May, 1956.
Saint Mary's Hospital
SENIOR HOUSE OFFICER for Pædiatric Department (53 Beds), including oversight of neonatal problems in a large Maternity Department. Vacant 16th May, 1956.
Royal Portsmouth Hospital (Orthopædic Department —104 Beds)
HOUSE OFFICER (pre-registration), vacant now.

Applications, stating age, experience, and qualifications, together with names of 2 referees, should be forwarded as soon as possible to E. H. HURST.
35, Grove-road South, Southsea.

PORTSMOUTH. ST. MARY'S HOSPITAL. Applications are invited for the appointment of SENIOR HOUSE PHYSICIAN at above Hospital. The duties will be mainly in medical wards that form an admission unit for 430 geriatric beds in the Group. A Consultant Physician being in charge of this unit. In addition the successful candidate will have duties in respect of 20 acute medical beds in the Hospital.

Applications, giving age, nationality, qualifications and experience, together with the names and addresses of 2 referees, should be sent to the Group Secretary, Portsmouth Group Hospital Management Committee, 35, Grove-road South, Southsea.

PAISLEY AND DISTRICT HOSPITALS BOARD OF MANAGEMENT. Applications are invited for JUNIOR HOSPITAL MEDICAL OFFICER posts at the following hospitals :—

(*a*) Orthopædic Unit, Royal Alexandra Infirmary, Paisley.
(*b*) Darnley Sanatorium, Nitshill, Glasgow.
(*c*) Johnstone Sanatorium, Johnstone.

Applications, stating age, date of qualification, experience, &c., should be submitted to Group Medical Superintendent, Royal Alexandra Infirmary, Paisley.

PEMBURY HOSPITAL, Pembury. Applications are invited for the post of RESIDENT ANÆSTHETIST (Senior House Officer). Post vacant 1st June, 1956. Tenable for 12 months in the first instance and is recognised for the D.A. and the F.F.A.R.C.S. National Health Service scale, less £150 p.a. for board, lodging, &c.

Apply to the Group Secretary, Tunbridge Wells Group Hospital Management Committee, Sherwood Park, Pembury-road, Tunbridge Wells.

READING COMBINED HOSPITALS. Area Department OF OBSTETRICS AND GYNÆCOLOGY. (100 Beds.) Applications are invited from registered medical practitioners, Male and Female, for the resident appointment of GYNÆCOLOGICAL HOUSE SURGEON at the Royal Berkshire Hospital, vacant 1st June and tenable for 6 months. Post recognised for M.R.C.O.G.

Write, stating age and qualifications with dates, nationality, and present appointment, with a copy of 1 recent testimonial, to Secretary.

READING AREA DEPARTMENT OF MEDICINE. Applications are invited from provisionally registered medical practitioners for resident post of HOUSE PHYSICIAN, vacant 1st June, and tenable for 6 months. Successful candidate will be required to carry out duties at following Reading hospitals : Royal Berkshire (399 Beds), Battle (391 Beds), and Prospect Park (104 Beds).

Write, before 19th May, stating age, qualifications with dates, nationality, present post, with copy of 1 recent testimonial, to Secretary, Royal Berkshire Hospital, Reading.

READING. ROYAL BERKSHIRE HOSPITAL. (399 Beds.) Applications are invited from provisionally registered medical practitioners, Male and Female, for resident post of HOUSE SURGEON, vacant 1st June, and tenable for 6 months.

Write, before 19th May, stating age, qualifications with dates, nationality, present post, with copy of 1 recent testimonial, to Secretary.

READING. ROYAL BERKSHIRE HOSPITAL. (405 Beds.) Applications are invited from registered and provisionally registered medical practitioners, Male or Female, for post of RESIDENT HOUSE SURGEON (E.N.T.), vacant immediately, for period of 6 months. Salary £425–£525 p.a., less £125 board-residence.

Write, stating age, qualifications with dates, nationality, present post, with copy of 1 recent testimonial, to Secretary.

REDHILL. EAST SURREY HOSPITAL, Shrewsbury-road, REDHILL, SURREY. SENIOR HOUSE OFFICER. Mainly general and orthopædic surgery, with some general medicines. Vacant 1st May.

Apply to Hospital Secretary, quoting 2 referees.

ROTHERHAM HOSPITAL, Doncaster Gate, Rotherham. (161 Beds. Recognised for training for the F.R.C.S. examination.) **SHEFFIELD REGIONAL HOSPITAL BOARD.** Whole-time RESIDENT REGISTRAR (orthopædics and casualty) required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 7th May, 1956, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

ROTHERHAM CLINICAL LABORATORY, Moorgate GENERAL HOSPITAL, ROTHERHAM. SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT or NON-RESIDENT REGISTRAR (pathology) required with duties at associated clinical laboratories within the area of the Rotherham and Mexborough Hospital Management Committee. Appointment for 1 year in the first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 7th May, 1956, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

ROCHFORD, ESSEX. GENERAL HOSPITAL. (603 Beds.) SENIOR HOUSE OFFICER required for Geriatric and Psychiatric Units at the above Hospital. Post vacant 23rd May, 1956. A wide range of facilities are available at the Hospital for the investigation, treatment and rehabilitation of acute and chronic cases. Possibility of accommodation for married applicant becoming available.

Applications, stating age, &c., to be sent to the undersigned by 5th May, 1956. J. C. FIELD, Secretary.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.) ORTHOPÆDIC HOUSE SURGEON (resident) required in the Orthopædic and Accident Unit. The service consists of 100 Beds equally divided between traumatic surgery and " cold " orthopædics. Post is recognised for pre-registration purposes and for F.R.C.S.

Applications to be sent to Group Secretary, Romford Hospital Management Committee, Oldchurch Hospital, as soon as possible.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.) SENIOR HOUSE OFFICER required in the Department of Ophthalmology from 22nd May, 1956.

Applications should be addressed immediately to the Group Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

ROMFORD, ESSEX. VICTORIA HOSPITAL. (99 Beds.) Temporary SURGICAL REGISTRAR (Male) required immediately.

Applications should be forwarded to Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

RICHMOND, SURREY. ROYAL HOSPITAL. (Acute General Hospital—121 Beds.) Applications are invited for the following posts.

NON-RESIDENT CASUALTY OFFICER (Senior House Officer grade). Post vacant as from 22nd June, 1956.

Pre-registration HOUSE PHYSICIAN. Post vacant as from 1st June, 1956.

Pre-registration HOUSE SURGEON. Post vacant as from 20th June, 1956.

Apply to Administration Officer.

SHEFFIELD. CITY GENERAL HOSPITAL. Department OF PATHOLOGY GROUP LABORATORY. Applications are invited for the appointment of SENIOR HOUSE OFFICER (clinical pathology). Resident accommodation is available and optional. Opportunities for training in morbid anatomy, biochemistry, hæmatology and bacteriology. The work at this and the associated hospitals offers excellent experience to graduates who wish to make pathology their permanent career. The post is recognised for the D.Path.

Apply, giving details of age, qualifications, present and previous appointments with dates, and the names of 2 persons to whom reference may be made, to the Group Secretary at Nether Edge Hospital, Sheffield, 11.

SHEFFIELD. CITY GENERAL HOSPITAL. (652 Beds. Recognised for D.Path.) **SHEFFIELD REGIONAL HOSPITAL BOARD.** Whole-time NON-RESIDENT REGISTRAR (pathology), required with duties at other hospitals in the Sheffield area. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 7th May, 1956, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. Applications are invited for the non-resident post of REGISTRAR or SENIOR HOUSE OFFICER in Clinical Pathology. Grade according to qualifications and experience. Post vacant 23rd July.

Applications, with the names of 3 referees, should be sent immediately to the Chief Administrative Officer, The United Sheffield Hospitals, West-street, Sheffield, 1.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the following appointments, which will be for 1 year in the first instance :—

REGISTRAR in Obstetrics and Gynæcology based at Braeholm Maternity Hospital, Helensburgh.

REGISTRAR in Surgery with duties in gynæcology based at the Royal Infirmary, Greenock.

REGISTRAR in Ophthalmology based at the Ophthalmic Institution, Glasgow.

REGISTRAR in Medicine based at the Royal Infirmary, Glasgow.

REGISTRAR in Dermatology based at the Western Infirmary, Glasgow.

REGISTRAR in Orthodontics based at the Glasgow Dental Hospital and School.

REGISTRAR in Pædiatrics for duties at Seafield Children's Hospital, Ayr, and at the Ayrshire Maternity Hospital.

REGISTRAR in Anæsthetics for duties at Killearn Hospital, Stirlingshire, and at the Western and Royal Infirmaries, Glasgow. This appointment at Killearn Hospital will be mainly for duty in the Neurosurgical Unit, and after 6 months the Registrar will continue in the Anæsthetic Department of the Western and/or Royal Infirmary on a rotational basis.

These appointments are subject to the National Health Service (Scotland) superannuation regulations.

Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, by 5th May, 1956.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the following appointments, which will be for 1 year in the first instance :—

SENIOR REGISTRAR in Anæsthetics based at the Western Infirmary, Glasgow.

SENIOR REGISTRAR in Bacteriology based at Stobhill Hospital, Glasgow.

REGISTRAR in Psychiatry based at the Glasgow Royal Mental Hospital.

These appointments are subject to the National Health Service (Scotland) superannuation regulations.

Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, by 12th May, 1956.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of a SENIOR REGISTRAR in the Regional Pool of Anæsthetists, based on the Royal Infirmary of Edinburgh. The successful candidate will be seconded for periods of duty in peripheral hospitals, details of which may be obtained on application.

Applications, stating age, qualifications and previous experience, together with the names of 3 referees, should be submitted to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, by 12th May, 1956.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of SENIOR REGISTRAR in Medical Pædiatrics at the Royal Hospital for Sick Children, Edinburgh, vacant on 23rd July, 1956.

Applications, giving particulars of age, qualifications and previous experience, together with the names of 3 referees, should be sent to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, by 19th May, 1956.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of REGISTRAR in the Regional Pool of Anæsthetists based on the Royal Infirmary of Edinburgh, vacant on 25th June, 1956. The successful candidate will be seconded for periods of duty in peripheral hospitals, details of which may be obtained on application.

Applications, stating age, qualifications and previous experience, together with the names of 2 referees, should be submitted to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, by 12th May, 1956.

SALISBURY GENERAL HOSPITAL. Applications are invited for the appointment of SENIOR HOUSE OFFICER to the E.N.T. Department. Post is recognised for D.L.O. and F.R.C.S., and is vacant early May.

Applications, naming 2 referees, to Group Secretary, Salisbury Group Hospital Management Committee, Odstock Hospital, Salisbury, Wilts.

SALISBURY GENERAL HOSPITAL. Applications are invited for the appointment of RESIDENT HOUSE SURGEON/HOUSE PHYSICIAN to run consecutively in this order from 1st July, 1956, for a period of 6 months in each post. The post is open to pre-registration candidates.

Apply, naming 2 referees, to Group Secretary, Salisbury Group Hospital Management Committee, Odstock Hospital Salisbury.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL (278 Beds) and SOUTHAMPTON GENERAL HOSPITAL (471 Beds). (Recognised for F.R.C.S.) RESIDENT HOUSE SURGEONS required beginning of June. Pre-registration candidates eligible.

Applications, with copies of recent testimonials, should be forwarded to Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHEND GENERAL HOSPITAL. Temporary Senior HOUSE OFFICER (Orthopædic and Fracture Departments) required from 16th May, 1956, or earlier on a month-to-month basis.

Applications, stating age, experience, &c., to be sent to the undersigned by 4th May, 1956. J. C. FIELD, Secretary.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire. Locum Tenens GYNÆCOLOGICAL AND OBSTETRIC REGISTRAR (resident) required for duties mainly at the above Hospital from 19th May, pending whole-time appointment.

Applications to Secretary, Mid Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans, as soon as possible.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire. (384 Beds.) Locum Tenens SURGICAL REGISTRAR (resident) required for 1 of the 2 general surgical teams for the period 5th–20th May inclusive.

Applications to Secretary Mid Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire. (384 Beds.) HOUSE PHYSICIAN (House Officer grade) required to 1 of the 2 medical teams for duties mainly on the acute wards. Post vacant about 24th May, and tenable for 6 months. Preference given to candidates seeking pre-registration posts under the Medical Act, 1950.

Applications to the Secretary, Mid Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

ST. HELENS AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of CASUALTY OFFICER in the Senior House Officer grade, at St. Helens Hospital (196 Beds). The post is approved for the 6 months training in casualty work required of candidates for the Fellowship examination of the Royal College of Surgeons.

Applications, stating age, qualifications, and experience, and giving 2 names for reference, should be forwarded immediately to N. RICHARDS, Group Secretary.

Whiston Hospital, Prescot.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. (455 Beds.) SENIOR HOUSE OFFICER in Orthopædics. Recognised F.R.C.S.

Applications, with names of 2 referees, to Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. HOUSE OFFICER (general surgery) required. Pre-registration post. Hospital recognised for F.R.C.S.

Detailed applications, with copy testimonials, to Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. STANFIELD SANATORIUM. (71 Beds—Tuberculosis.) JUNIOR HOSPITAL MEDICAL OFFICER required. Resident.

Applications to Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

TORQUAY. TORBAY HOSPITAL. Senior Resident HOUSE OFFICER (medicine) required immediately. There is a complement of 5 Resident House Officers.

Applications, stating qualifications, age, nationality, with copy testimonials (quoting ref. F.955/68) to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, S. Devon.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. SENIOR HOUSE OFFICER (anæsthetics) required. Post which is tenable for 1 year, will be resident.

Applications, with names of 2 referees, to Secretary.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. RESIDENT MEDICAL REGISTRAR required, 1st June, at above Hospital.

Application forms from, and returnable to, Secretary, Windsor Group Hospital Management Committee, Alma-road, Windsor, by 4th May.

WAKEFIELD. PINDERFIELDS GENERAL HOSPITAL. SENIOR HOUSE OFFICER required for Orthopædic Department. Salary £745 p.a. Residential accommodation at charge of £155 p.a.

Written applications, giving full details of experience, &c., and 2 names and addresses for reference, to—

W. BOWRING, Group Secretary.

Victoria Chambers, Wood-street, Wakefield.

WARRINGTON INFIRMARY. (172 Beds.) Applications are invited for the post of RESIDENT CASUALTY OFFICER (Male or Female), vacant in early May. The post is graded Junior Hospital Medical Officer. Scale of salary £775 by £50 rising to £1075, less deduction of £130 for residential emoluments. Applications will also be considered from Junior Medical Officers who would be graded House Officer or Senior House Officer at the scale appropriate to the experience of the applicant. Consideration will also be given to applicants who desire the appointment on a short-term basis. A whole-time Senior Hospital Medical Officer is in charge of the Department.

Applications, stating age, experience and qualifications should be forwarded or telephoned to—

H. L. BOOT, Group Secretary,
Warrington and District Hospital Management Committee.
c/o General Hospital (Tel. No. Warrington 1666).
Warrington, Lancs.

WARRINGTON INFIRMARY. (172 Beds.) Applications are invited from persons experienced in anæsthetics for the post of RESIDENT ANÆSTHETIST (Male or Female). Graded as Senior House Officer. The Hospital is recognised for the D.A. examination. Salary is £745 p.a., less a deduction of £130 p.a. for residential emoluments.

Applications, stating qualifications and experience, should be sent to— H. L. BOOT, Group Secretary,
Warrington and District Hospital Management Committee.
c o General Hospital, Warrington, Lancs.

WELSH REGIONAL HOSPITAL BOARD.

SENIOR REGISTRAR in General Surgery. Based at Royal Gwent Hospital, Newport (260 Beds) to serve other hospitals in Group. Non-resident. Appointment for period of 2 years in first instance.

REGISTRAR (general surgery), Pembroke County War Memorial Hospital, Haverfordwest. Resident or non-resident.

REGISTRAR in Psychiatry, North Wales Hospital for Nervous and Mental Disorders, Denbigh. Hospital provides comprehensive mental health service for North Wales. Outpatient clinics at major general hospitals and associated child guidance services. Every modern therapy and Department of Psychology and Electroencephalography. Modern open-door reception units with annual admission rate over 800. Small flat available suitable for single man or man and wife only.

REGISTRAR (general surgery). To serve Newport and East Mon Hospital Management Committee. Based at Royal Gwent Hospital, Newport (260 Beds). Non-resident.

Subject to review end of first year.

Application forms from Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 14 days.

WEST MALLING, KENT. LEYBOURNE GRANGE COLONY FOR MENTAL DEFECTIVES. (1445 Beds.) JUNIOR HOSPITAL MEDICAL OFFICER required at above Colony. Salary scale £775–£50–£1075 a year. Appointment is subject to the terms and conditions of service for medical and dental staffs and is for a period of 3 years in the first instance. Furnished or unfurnished married accommodation available. Ample facilities for study.

Applications, with full details as to age, nationality, qualifications, present post and previous experience, together with names and addresses of 2 referees, to the Group Secretary by 9th May, 1956.

WHITEHAVEN HOSPITAL, Cumberland. (124 Beds and Annexe of 27 Beds.) HOUSE OFFICER (obstetrical and gynæcological). House Officer or Senior House Officer grade. Vacant beginning of May.

Detailed applications, with dates and names of 2 referees, to the Group Secretary, Workington Infirmary, Cumberland.

WICKFORD (near), ESSEX. RUNWELL HOSPITAL. (1032 Beds.) SENIOR HOUSE OFFICER (Male or Female) required for 1 of the Consultant's Divisions and to assist in outpatient work. Excellent postgraduate facilities for D.P.M. Salary £745 ; residential charge £180.

Applications, with copies of testimonials, to the Secretary.

WOODFORD BRIDGE, WOODFORD GREEN, ESSEX. CLAYBURY HOSPITAL (for mental and nervous disorders). Applications are invited for the post of Full-time SENIOR HOUSE OFFICER (resident or non-resident). Board residence for an unmarried applicant, for which a charge of £170 p.a. will be made, is available. The Hospital has over 2000 Beds and an admission-rate of over 1300 a year. All forms of treatment are undertaken and outpatients clinics at general hospitals are run by the Hospital staff. Clinical conferences and seminars for the D.P.M. candidates are held weekly and facilities will be offered to attend lectures in London (1 hours journey). Previous general, but not psychiatric experience necessary.

Applications, with full particulars and the names and addresses of 2 referees, to be sent to the Physician-Superintendent not later than 14 days after the appearance of this advertisement.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOSPITAL. (315 Beds.) HOUSE SURGEON (post recognised by Royal College of Surgeons) required for general surgery with some E.N.T. duties. Approved pre-registration post. Vacant 1st June.

Applications, with copies of 2 testimonials, to the Group Secretary.

WINDSOR. KING EDWARD VII HOSPITAL. House PHYSICIAN required (Male or Female) for post vacant 15th June. Preference given to persons seeking a pre-registration post. Applicants required to be members of a Medical Protection Society.

Applications, stating age, qualifications with dates, and nationality, with copies of 3 recent testimonials, to Secretary

WREXHAM WAR MEMORIAL HOSPITAL. (230 Beds.) WREXHAM, POWYS AND MAWDDACH HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER (resident or non-resident) for the Casualty Orthopædic Department of the above Hospital. The appointment is recognised for the Diploma of F.R.C.S. (Eng. and Edin.), and is subject to a limited tenure of 2 years, which may be reviewed at the end of that period. Salary £775–£50–£1075 p.a. Whitley Council conditions of service.

Applications, giving details of age, qualifications, and previous experience, together with copies of 2 recent testimonials, should be sent to the Group Secretary, Maelor General Hospital, Wrexham, as soon as possible.

CHANNEL ISLANDS, JERSEY. GENERAL HOSPITAL. Applications are invited for the post of RESIDENT SURGICAL OFFICER at the above Hospital. Previous experience is essential. The Hospital has 200 Beds and is recognised as a training hospital for the F.R.C.S. Post is vacant on 16th June, 1956. The appointment is for 6 months in the first instance, but is renewable for a further 6 months. Salary £850 p.a., less £125 for residential emoluments.

Applications to be submitted not later than 17th May, 1956, to the President, Public Health Committee, General Hospital, Jersey, C.I.

BELFAST HOSPITAL MANAGEMENT COMMITTEE, Riddel House, ROYAL VICTORIA HOSPITAL, BELFAST. SENIOR HOUSE OFFICERS required for the period to 30th September, 1956, for the following posts :—

(*a*) General Surgery.
(*b*) Anæsthesia.
(*c*) Radiology.

Salary £745 p.a.

Application to be made on a form obtainable from the Secretary, Belfast Hospital Management Committee, Riddel House, Royal Victoria Hospital, Belfast.

DUBLIN. NATIONAL CHILDREN'S HOSPITAL, 88, Harcourt-street. The post of MEDICAL REGISTRAR will be vacant on 1st June, 1956. Salary £550, less £150 p.a.

Applications, with copies of testimonials, must reach the House Governor by 10th May.

NORTHERN IRELAND HOSPITALS AUTHORITY. Appointment of REGISTRARS, TUTORS/REGISTRARS and JUNIOR TUTORS/SENIOR HOUSE OFFICERS. Applications are invited for whole-time posts as Registrar in hospitals in Northern Ireland for the period 1st October, 1956–30th September, 1957. Vacancies will occur in all specialties, and appointments will be made in either of 2 grades, viz., Senior Registrar or Principal Registrar, the analogous grades in Great Britain being Registrar and Senior Registrar. Some of the appointments will be made jointly by the Queen's University, Belfast, and the Authority, and will involve teaching and other University duties as Senior or Principal Tutor. There will also be vacancies for whole-time Junior Tutors/Senior House Officers for the same period.

Applications should be made on a form which may be obtained (with further particulars) from the Secretary, Northern Ireland Hospitals Authority, 44–46, Queen-street, Belfast, and which must be returned so as to be received not later than 12th May, 1956.

Public Appointments

STAFFORDSHIRE COUNTY COUNCIL. Applications are invited from fully qualified medical practitioners for the appointment of ASSISTANT COUNTY MEDICAL OFFICER AND SCHOOL MEDICAL OFFICER, the main duty of which will be the administration of dental anæsthetics, so that previous experience in that connection will be an advantage. Other duties will be prescribed by the County Medical Officer of Health as and when required. The salary scale is £975–£50–£1375, and previous Local Authority Service may be taken into consideration when deciding the commencing rate. The use of a car will be necessary and allowances will be paid in accordance with the County Council scale. The appointment will be terminable by 3 months notice in writing on either side and superannuable, and the selected candidate will be required to pass a medical examination and produce his or her birth certificate.

Forms of application and further information can be obtained from the County Medical Officer of Health, County Buildings, Stafford, to whom applications should be sent by not later than 12th May, 1956.

T. H. EVANS, Clerk of the County Council.

County Buildings, Stafford, 17th April, 1956.

LANCASHIRE COUNTY COUNCIL. Applications invited from registered medical practitioners for appointment of ASSISTANT DIVISIONAL MEDICAL OFFICERS in the Boroughs of Eccles, Lytham St. Annes and in areas adjacent to Oldham and St. Helens-Warrington. Possession of D.P.H. desirable. Salary £975–£1375 p.a. Travelling and subsistence allowances where applicable.

Application forms and further particulars from County Medical Officer, Serial 553, East Cliff County Offices, Preston.

BRADFORD. CITY OF BRADFORD. Health Department. Applications are invited from registered medical practitioners for the appointment of ASSISTANT MEDICAL OFFICER. The successful applicant will be employed mainly on school health and maternity and child welfare work and may be required to undertake other duties from time to time as decided by the Medical Officer of Health. If the successful candidate does not possess the Diploma in Public Health he will be expected to avail himself of facilities which may be given to take the course for such Diploma on a part-time basis at Leeds University. Salary is in the scale £975–£50–£1375, according to experience, &c. The post is subject to the appropriate superannuation scheme and the successful candidate will be required to pass a medical examination.

Forms of application and further particulars may be obtained from the Medical Officer of Health, Town Hall, Bradford, and should be returned to the undersigned within 14 days of the appearance of the advertisement.

W. H. LEATHEM, Town Clerk.

Town Hall, Bradford, 12th April, 1956.

BARBADOS GENERAL HOSPITAL. Medical Officers are required at the General Hospital, Barbados, to undertake duties ordinarily performed in a large acute general hospital of 500 Beds, including medical, surgical, obstetrics, theatre and ward work, anæsthetics, casualties and outpatients and any other departmental duties as may be directed. Candidates must possess qualifications registrable in the United Kingdom. Appointments will be on agreement for 3 years ; or (if the officer is a bachelor) on 1 year agreement, renewable—with return passage. Salary scale is $3720–$4920 (£775–£1025) a year, starting salary depending upon candidates age and experience. A temporary cost-of-living allowance of $156 (£32 10s.) a year is also payable. The Government of Barbados would pay employer's share of contributions to an approved superannuation scheme during period of Officer's service there. Free quarters are provided and furniture, linen, cutlery and crockery. Free passages to Barbados are provided for the Officer, wife, and children on first appointment and back to the United Kingdom on the satisfactory completion of the agreement, subject to a total maximum cost of $1440 (£300) each way. Income-tax at local rates. Social and recreational amenities are good. Climate is healthy. Educational facilities are available.

Application forms from Director of Recruitment, Colonial Office, Sanctuary Buildings, Great Smith-street, London, S.W.1 (quoting reference No. BCD.117/28/02).

HER MAJESTY'S OVERSEA SERVICE. Medical Branch —TANGANYIKA. MEDICAL OFFICERS with qualifications registrable in the United Kingdom are required in Tanganyika for general duties. Officers would normally be based on a hospital but must be prepared to tour and to assist in training African staff. There is 1 vacancy for which an officer possessing the F.R.C.S. is required ; he would be regarded as available for general medical duties but would be allotted surgical work as far as possible. Appointments can be made on a permanent basis with pension (non-contributory), or on short-term contract with gratuity payable on satisfactory completion of service. A doctor in the National Health Service may leave the National Health Service but retain his superannuation rights (up to a limit of 6 years) and receive a gratuity (taxable) of 20% of the aggregate of his salary after his engagement. Salary ranges from £1116 to £1836 a year ; starting point is determined by experience and 4 extra increments are given to successful candidates possessing the F.R.C.S., M.R.C.P., D.P.H., or other approved higher qualifications. Temporary cost-of-living allowance at the rate of 10% of salary is also payable, subject to a maximum of £162 a year, making gross emoluments of £1228–£1998 a year. Permanent Medical Officers are eligible to be considered at any time for promotion to super-scale posts in Tanganyika and other territories in medical administration or, if they possess higher qualification and suitable experience, in specialist posts. Quarters are generally available at rental varying from £30 to £78 a year according to size and type, and furniture at a rate varying from £12 to £24 a year. Free passages in both directions for Officer and wife and up to cost of 1 adult fare for children. Taxation at local rates. Annual local leave permissible and generous home leave granted after each tour of from 30 to 36 months. Educational facilities are available.

Application forms from Director of Recruitment, Colonial Office, Sanctuary Buildings, Great Smith-street, London, S.W.1 (quoting reference No. BCD.117/8/02).

SUDAN GOVERNMENT. The Ministry of Health, Sudan Government, invites applications for the following posts :—

BACTERIOLOGIST. Candidates should have specialist experience in bacteriology, and in a reputed Institute. Salary ranges from £E1750 to £E2330 p.a. (for Junior Specialist) or a fixed salary of £E2500 p.a. (for Specialist).

Male SPECIALIST SURGEONS AND GYNÆCOLOGISTS. Candidates must possess adequate professional qualifications for the type of post, viz., M.R.C.P., F.R.C.S., or M.R.C.O.G. Age should be 28–43. Salary ranges from £E1750 to £E2330 p.a. (for Junior Specialists) or fixed rate of £E2500 p.a. (for Specialists).

Candidates for these posts may apply for secondment from the National Health Service for a period of up to 3 years under the terms of circular letter No. RHB/(52)106EG(52)101 of 30th September, 1952.

All the above appointments will be on short-term contracts for a period of up to 3 years and starting-rates of pay will be determined according to age, experience and qualifications. In certain cases a cost-of-living allowance is also payable at present. A bonus of 1 months salary for each year of service, subject to a maximum of 6 months pay is payable on satisfactory completion of the contract. Outfit allowance of £E50 is payable when the contract is signed. Free passage on appointment. Annual leave after the first tour.

Further particulars and application form will be sent on application to Dr. E. P. PRATT, Consultant Physician to the Sudan Government, 137, Harley-street, London, W.1.

DUNDEE. CORPORATION OF DUNDEE. Public Health DEPARTMENT. Applications for the post of ASSISTANT MEDICAL OFFICER OF HEALTH (Male) are invited from registered medical practitioners. Applicants should be under 45 years of age unless in the employment of another Authority paying a transfer value. Preference will be given to applicants possessing a Diploma in Public Health. Duties are mainly in connection with Public Health Preventive Services—executive and administrative. Further details can be obtained from the Medical Officer of Health, 9, West Bell-street, Dundee. Salary will be in accordance with national scale with placing according to experience. The appointment is superannuable and the successful candidate will be required to pass a medical examination.

Applications, stating age, qualifications and experience, and giving the names and addresses of 3 referees, should be lodged with the subscriber on or before 11th May, 1956.

City Chambers, Dundee. ROBERT LYLE, Town Clerk.

GOLD COAST LOCAL CIVIL SERVICE. Gold Coast MEDICAL SERVICE. Applications are invited from doctors with registrable qualifications for the following posts in the Gold Coast Local Civil Service :—

(1) MEDICAL OFFICERS for general duties including hospital and district work.

(2) MEDICAL OFFICERS OF HEALTH to prevent disease and to carry out treatment whenever necessary. Candidates must possess in addition to registrable qualifications the Diploma of Public Health or a similar recognised qualification.

Appointment may be as follows :—

(a) Contract for 2 tours of duty of 18–24 months with gratuity (taxable) at the rate of £12 10s. for each completed month of service. Salary in the scale £1330–£2310 a year.

(b) On 3-years probation for permanent and pensionable employment. Pension (non-contributory) is earned at the rate of 1/600th of the final pensionable emoluments for each completed month of service. Salary in the scale £1055–£1850 a year.

(c) Doctors in the National Health Service may leave the National Health Service but retain their superannuation rights while in the Gold Coast (up to 6 years) and receive a gratuity (taxable) of 20% of their Gold Coast salary after their engagement. Salary in the scale £1055–£1850 a year.

Starting point in salary scales is determined according to qualifications and experience.

Quarters are provided at rental not exceeding £150 a year. Income-tax at local rates. Free passages provided for Officer, wife, and up to 3 children under 13 years of age. Annual local leave is permissible and generous home leave is granted after each tour.

Application forms can be obtained from the Director of Recruitment Colonial Office, Sanctuary Buildings, Great Smith-street, London, S.W.1 (quoting reference No. BCD.117/13/04).

STAFFORDSHIRE COUNTY COUNCIL. Darlaston URBAN DISTRICT COUNCIL. Applications are invited for the part-time appointments of ASSISTANT COUNTY MEDICAL OFFICER AND SCHOOL MEDICAL OFFICER, AND MEDICAL OFFICER OF HEALTH of the Darlaston Urban District. These appointments together will constitute whole-time, the allocations being 7 half-days and 4 half-days, respectively. The proportionate salaries for the appointments, in accordance with the latest Industrial Court Award, are:—

Assistant County Medical Officer, &c. (County Council) :—£709 1s. 10d.–£36 7s. 3d.–£1000.

Medical Officer of Health (Darlaston U.D.) :—£627 5s. 5d.–£19 1s. 10d.–£703 12s. 9d.

Increments will be given for previous service in the same capacity.

These appointments will be subject to the provisions of the Local Government Superannuation Acts, 1937–53, and the successful candidate will be required to pass a medical examination and to produce his or her birth certificate. Applicants must be fully qualified medical practitioners with experience in public health duties and must hold the Diploma of Public Health. The candidate appointed will, as regards the County Council duties, act under the direction of the County Medical Officer of Health and will be required to perform such duties as may from time to time be prescribed. As regards the duties as District Medical Officer of Health he or she will be subject to the Sanitary Officers (Outside London) Regulations, 1935 and 1951, and to the sole control and direction of the Local Sanitary Authority. The County Council appointment will be subject to 3 calendar months notice in writing on either side.

Forms of application may be obtained from the Clerk of the County Council and should be returned to the County Medical Officer of Health, County Buildings, Stafford, by first post on 12th May, 1956, together with copies of not more than 3 recent testimonials.

T. H. EVANS, Clerk of the County Council.
G. R. ROWLANDS,
Clerk of the Darlaston Urban District Council.

County Buildings, Stafford, 5th April, 1956.

General Practice

For an Executive Council post (England and Wales) apply on form E.C.16A obtainable from the council. Mark envelope "Vacancy."

MITCHAM, SURREY. Applications invited for Vacancy due to death in above borough (intermediate). List about 2100. Residence and surgery may be available for purchase and branch surgery to rent. Applications on Form E.C.16A, to reach the undersigned not later than 11th May, 1956.

S. H. BENNETT, Clerk of the Council.

187, Ewell-road, Surbiton.

Hospital Services : Non-Medical Appointments

CHESTER BEATTY RESEARCH INSTITUTE, Institute OF CANCER RESEARCH : ROYAL CANCER HOSPITAL, Fulham-road, S.W.3. SENIOR TECHNICIAN (grade II) required, with experience and training in histology. A basic knowledge of haematology and bacteriology, although not essential, would be regarded as an asset. A qualification of the Institute of Medical Laboratory Technicians would also be an asset but is not essential. The post is superannuable and the salary will be in accordance with the new Whitley Council scales.

Applications, marked "Histology" and including the names of 2 referees, should be sent to the Secretary, not later than 31st May, 1956.

Miscellaneous

To non-professional posts the Notification of Vacancies Order 1952 applies

Boots Pure Drug Co. Ltd. have a vacancy in the Biology Division of the Research Department for a Senior Research Pharmacologist for long term research work of considerable interest. This is a senior position, and applicants (age under 40 years) should have had some years research experience.—Applications should be addressed to the Personnel Manager, Boots Pure Drug Co. Ltd., Station-street, Nottingham.

Boots Pure Drug Co. Ltd. invite applications from registered medical practitioners for an appointment as Assistant Medical Adviser in the Medical Department of Boots Pure Drug Co. Ltd. The functions of this Department include a close collaboration with the Research Department, the organisation of clinical trials, the provision of a comprehensive medical information service and the supervision of medical literature. Applicants must have had several years clinical experience, should have an extensive knowledge of medicine and some experience of clinical or laboratory research. A practical knowledge of tropical medicine would be an advantage.

Applications and requests for further details should be sent to the Head of the Medical Department, Boots Pure Drug Co. Ltd., Station-street, Nottingham.

Australian Red Cross Society. New South Wales Division. Applications are invited for the position of Assistant Director in the Blood Transfusion Service. The position is full-time without the right of private practice and the salary is £2500 p.a. Australian currency. The successful applicant will be expected to assist the Director in the supervision of blood collection and laboratory procedures. Experience in laboratory methods is essential.

Written applications should be addressed to the General Secretary of the Australian Red Cross Society, New South Wales Division, 27, Jamison-street, Sydney, N.S.W., and should state age, academic record, war service (if any) and post-graduate experience, especially in laboratory methods.

Applications invited for position in Medical Information Department of leading Pharmaceutical House in West End of London—good knowledge of pharmacy and therapeutics with aptitude for writing. Age not over 40. 5-day week ; contributory pension scheme.—Full particulars of qualifications and experience to : Address, No. 210, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Rural practice in Somerset, easy reach of coast. Light work. Car provided if necessary. Standard fees. Male or female. Comfortable accommodation provided. 10th June–30th June.—Apply: Dr. M. D. THOMSON, The Tower House, Chilton Polden, Somerset.

Qualified Sister requires Medical-Receptionist-Secretarial post with Doctor. London. Excellent references.—Address, No. 217, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Wanted part-time Assistant (Lady preferred) West London. Car essential.—Address; No. 214, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Large first-floor consulting-room in Harley-street area to be let furnished, part-time, with full service and secretarial facilities.—Apply : Address, No. 215, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Queen Anne-street consulting-room available part-time. —Write : Address, No. 216, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

The British Journal of Medical Hypnotism. Quarterly, £1 1s. p.a.—Orders to the publishers, 4, Victoria-terrace, Hove, 3, Sussex.

"Pregnancy Diagnosis by the Xenopus Method," 24-hour service. Send specimen of urine and £1 1s. fee. Hæmatology, Biochemistry, Flame Photometry.—WELBECK BIOLOGICAL LABORATORIES, 26, Park-crescent, Portland-place, W.1 (MUSeum 5386–7).

Applicants for posts requiring testimonials copied or duplicated should communicate with MANTON SECRETARIAL SERVICE LTD., 98, Victoria-street, S.W.1 (Phone : VICtoria 0141), who are specialists in this kind of work.

Typewriting and Duplicating. First-class work at moder-ate prices by experienced medical typists. Electric machines. —SYBIL RANG, 21, Heath-street, Hampstead, London, N.W.3 (HAM 5329/0504).

Austin House offer limited number new car deliveries at reduced hire purchase and insurance rates to proven essential user members of Medical Profession. Brochures, application forms free.—Austin House, 142, Golders Green-road, Golders Green, London, N.W.11.

Microscopes. Highest prices paid for good modern types. Send or bring your equipment for valuation.—WALLACE HEATON LTD., 127, New Bond-street, W.1.

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1. LANCET, 1954, 2, 942.
2. B.M.J., 1954, 2, 1257.
3. B.M.J., 1954, 2, 1255.
4. LANCET, 1954, 2, 1245.

IMFERON IS THE FIRST EFFECTIVE IRON PREPARATION FOR INTRAMUSCULAR INJECTION

IT PROVIDES the rapid, reliable response of an order hitherto only obtainable with intravenous preparations; and it takes much less time to administer.

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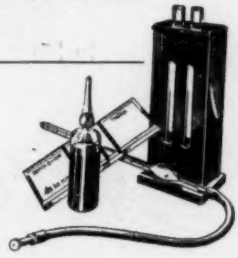
(Lancet, 1954, 2, 1245).



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